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Document Title	LETTER FROM BASF CORP TO USEPA RE: REPORT ON THE STUDY OF PALATINOL A (DEP) (ZST TEST SUBSTANCE NO. 92/187) IN THE AMES TEST W/ATTACHMENTS & COVER LETTER DATED 05/06/94 (SANITIZED)		
Chemical Category	PALATINOL A (CAS# 84-66-2)		

CODING FORM FOR GLOBAL INDEXING

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BASF Corporation

BASF

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May 6, 1994

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869400003905

Attention: 8(D) Health and Safety Reporting Rule Notification
TSCA Document Processing Center (7407)
Office of Prevention, Pesticides and Toxic Substances
Environmental Protection Agency
401 M St. SW. Washington DC 20460

Subject: TSCA Section 8(D): Reporting of Health and Safety Information

9 MAY 11 AM 746
RECEIVED
OPPT/CBIC

Ladies and Gentlemen:

BASF Corporation is hereby submitting copies of all available health and safety information on Diethyl Phthalate (CAS # 84-66-2) also called Palatinol® A and Tetrahydrofuran (CAS #109-99-9) subject to the reporting in accordance with 40 CFR part 716, Federal Register Notice of February 9, 1994 (FR Vol. 59, No. 27). Attached please find all the study reports and/or health and safety data available at BASF Corporation.

For Tetrahydrofuran BASF Corporation is cosponsoring two testing programs which are currently in progress. Please refer to Attachment I for the details. No claims of confidentiality are being made on this submission.

CAS Registry # 84-66-2 Diethyl Phthalate (Palatinol® A)
CAS Registry # 109-99-9 Tetrahydrofuran

Submitting Site: BASF Corporation
8 Campus Drive
Parsippany, NJ 07054

Submitting Official: Dr. Sree L. Jasti
Toxicologist
1609 Biddle Avenue
Wyandotte, MI 48192

Please contact me if there are any questions regarding these submissions at (313) 246-5107.

Sincerely,
BASF CORPORATION

Sree Jasti

Sree L. Jasti, Ph.D.
Toxicologist

86940000381

TO

86940000391

ATTACHMENT I

STATUS OF ONGOING STUDIES ON TETRAHYDROFURAN (CAS # 109-99-9)

I Two Generation Reproduction Study of Tetrahydrofuran in Rats via Drinking Water:

The study is co-sponsored by BASF Corporation, ARCO Chemical Company and E.I. du Pont de Nemours and Company.

Study initiated on February 14, 1994. The purpose of this study is to evaluate the reproductive effects of tetrahydrofuran given orally via drinking water. The in-life phase of the study is expected to be complete by the end of January 1995. The final report is expected by May 1996.

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A one-generation range-finding study was conducted for this program in December 1993. The final report has just been received and is enclosed along with the other THF tox reports included in this submission.

The name and the address of the laboratory conducting the study is as follows:

BASF Aktiengesellschaft
Department of Toxicology
D-67056 Ludwigshafen/Rhein, FRG

II Acute and Sub-Chronic Neurotoxicity Studies By Vapor Inhalation

The studies are being conducted under a TSCA Section 4 Neurotoxicity End Point Rule by the Tetrahydrofuran Task Force. The THF Task Force is comprised of the following companies: ARCO Chemical Company, BASF Corporation, E.I. du Pont de Nemours and Company, GE Plastics, ISP Corporation and QO Chemicals.

The acute study has been completed, but a final report is not available yet. It will be forwarded upon receipt. The Tetrahydrofuran Task Force sent in a letter dated March 9, 1994, outlining study findings to fulfill TSCA section 8 (e) -- Notification of Substantial Risk to Health or Environment. The final report under Section 4 is due on September 9, 1995. The subchronic neurotoxicity studies will evaluate motor activity, functional observational battery and neuropathology and the final report is due September 9, 1996.

The name and address of the lab conducting the studies are as follows:

Du Pont Central Research & Development
E.I. Du Pont De Nemours and Company
Haskell Laboratory for Toxicology & Industrial Medicine
P.O. Box 50, Elkton Road
Newark, Delaware 19714

CAS No. 109-99-9 Tetrahydrofuran

1. Ames-Test for Tetrahydrofuran; ZHT-Bericht 77/952 vom 31.01.79 86940000381
2. Ames-Test for Tetrahydrofuran (stabilized by BHT); ZHT-Bericht 86940000382
77/953 vom 31.01.79
3. Bericht über die Prüfung der akuten Inhalationsgefahr (akutes Inhalationsrisiko) von "THF = Tetrahydrofuran p.A. (99,5 %), MERCK" an Sprague-Dawley-Ratten; ZHT-Bericht 78/785 vom 03.12.79 86940000383
4. Bericht über die orientierende Prüfung der Reizwirkung dreier Tetrahydrofuran-Gemische; ZHT-Bericht III/323-325, 328 vom 24.07.53 86940000384
5. Bericht über die eingehende toxikologische Prüfung von Tetrahydrofuran.
I. Teil: Akute Toxizität im Vergleich zu Diäthyläther, Äthanol, Aceton und
Dioxan. ZHT-Bericht vom 24.06.58 86940000385
6. Bericht über die vergleichende Prüfung der Reizwirkung von Tetrahydrofuran
und Cyclohexanon (= Anon). ZHT-Bericht II/274 vom 10.07.53 86940000386
7. Zeller, H. et al.: Zur Toxizität von Tetrahydrofuran. Naunyn-Schmiedebergs
Arch. exp. Path. Pharmak. 217, 359 - 360 (1964) 86940000387
8. Thiess, A.M. et al: Cytogenetic Investigation of Occupational Exposure
to Dioxane and Tetrahydrofuran. Medicem Proc. of the Eight Internat.
Conf. of Occupational Health in the Chemical Industry, Tokyo/Japan,
22.-25.09.80 (p. 102 - 109) 86940000388

86940000390

CAS No. 84-66-2 Diethyl phthalate



86940000390

1. Report on the Study of Palatinol A (DEP) in the Ames Test
(Salmonella/Mammalian-Microsome Mutagenicity Test - Standard Plate Test and Preincubation Test). ZHT-Bericht 92/187 vom 17.06.93

Confidential

BASF

Abteilung Toxikologie
Department of Toxicology
D-W6700 Ludwigshafen, FRG

en-bh; 2156
JUN 17 1993

REPORT
on the Study of
Palatinol A (DEP)
(ZST Test Substance No.: 92/187)

in the
AMES TEST

(Salmonella/Mammalian-Microsome
Mutagenicity Test - Standard Plate Test
and Preincubation Test)

Project No.: 40M0187/924111

Testing facility: BASF Aktiengesellschaft
Department of Toxicology, Z 470
D-W6700 Ludwigshafen/Rhein, FRG

Head of Department
of Toxicology: Prof. Dr.med. Dr.rer.nat. H.-P. Gelbke

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Project No. 40M0187/924111

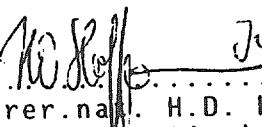
GLP STATEMENT

Title: Report on the Study of Palatinol A (DEP) in the AMES TEST
(Salmonella/Mammalian-Microsome Mutagenicity Test -
Standard Plate Test and Preincubation Test).

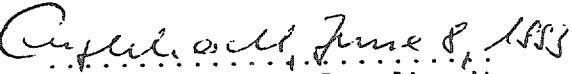
This study was conducted in accordance with the GLP-provisions of
the "Chemikaliengesetz" (Chemicals Act; Bundesgesetzblatt 1990,
Teil I, 22.03.90; FR Germany) and with the "OECD Principles of
Good Laboratory Practice" (Paris, 1981).

However, there was the following deviation from the requirements
of the above mentioned principles:

- Analytical investigations (stability of the test substance in
DMSO and aqua dest.) were not carried out.


June 14, 1993

Dr. rer. nat. H.D. Hoffmann
(Head of Section)


August 21, 1993

Dr. rer. nat. G. Engelhardt
(Study Director)

BASFAbteilung Toxikologie
Department of ToxicologyProject No. 40M0187/924111

STATEMENT OF THE QUALITY ASSURANCE UNIT

Number of test substance: 92/187

Name of test substance: Palatinol A (DEP)

Title: Report on the Study of Palatinol A (DEP)
in the AMES TEST (Salmonella/Mammalian-
Microsome Mutagenicity Test - Standard
Plate Test and Preincubation Test)

The Quality Assurance Unit performed the inspections given below,
and reported findings to the Study Director and to Management. The
conduct of this short-term study was not inspected; the processes
of the laboratory and of the study involved are inspected in
regular intervals.

Phase of study/ inspection	Date of inspec- tion	Report to Study Di- rector and to Manage- ment
Protocol:	July 16, 1992	Jan. 14, 1993
Audit of the report:	Jan. 14, 1993	Jan. 14, 1993

Ludwigshafen, June 17, 1993 *U. Wandelt-Hoetzl*
U. Wandelt-Hoetzl
(Quality Assurance Unit)

Vertraulich

→ Corialfarben

BASF

Abteilung Toxikologie
Department of Toxicology
6700 Ludwigshafen
West Germany

en-bh: 332 02. SEP. 1987

MITTEILUNG

über die Prüfung von

Corial Finish EC

(ZNT Substanz-Nr.: 87/469)

im
AMES-TEST

(Standard plate test
mit *Salmonella typhimurium TA 98 und TA 100*)

Projekt Nr.: 40M0469/874072

Diese Mitteilung besteht aus 2 Seiten und 4 Tabellen.

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Projekt Nr.: 40M0469/874072

ZUSAMMENFASSUNG

Die Substanz Corial Finish EC (ZNT-Nr.: 87/469) wurde im Ames-Test untersucht.

Stämme: TA 98, TA 100, TA 1535, TA 1537

Dosisbereich: 20 µg - 5000 µg/Platte

Testbedingung: Standard plate test ohne und mit metabolischer Aktivierung (Ratten S-9 Mix).

Löslichkeit: Vollständige Löslichkeit der Testsubstanz in DMSO.

Toxizität: Eine bakteriotoxische Wirkung (reduziertes his Backgroundwachstum) war nicht zu beobachten.

Mutagenität (Tabellen 1 - 2):

TA 98:

Keine Erhöhung der Zahl der

his Revertanten

TA 1535:

TA 100:

Bewertung:

Nach den vorliegenden Untersuchungsergebnissen wirkt die Substanz Corial Finish EC unter den gewählten Versuchsbedingungen nicht mutagen im Ames-Test.

 99.87 Aufgeschaut, oc. o. o. o.
Prof. Dr.med. Dr.rer.nat. H.-P. Gelbke Dr.rer.nat. G. Engelhardt
(Versuchsdurchführung)

R.A.S.F. A.G.
DEPARTMENT OF TOXICOLOGY

AMES TEST WITH 87/469
METHOD : STANDARD PLATE TEST

TABLE - 1

STUDY NUMBER: 874072
STUDY DIREC. : ENC
OPERATOR : SCH
DATE : 31.07.87
STRAIN: TA1535

DOSE MCG/PL	REVERTANTS / PLATE				TITER DIL		QUOTIENT	
	-S9	M	SD	+S9*	M	SD	EXP-6	-S9
NEGATIVE CONTROL	14 21	17 15	4 3	20 16	16 16	3 3	27 43 31	1.0 1.0
DMSO	16			14				
20	15 12 13	13 18 14	2 1 1	27 18 14	20 18 14	7 7 7		0.8 1.2
100	22 16 14	17 13 14	4 3 3	14 13 24	17 16 16	6 5 5		1.0 1.0
500	12 11 14	12 13 17	2 1 1	17 13 17	16 16 16	2 2 2		0.7 1.0
2500	11 17 15	14 17 14	3 3 3	13 17 14	15 17 14	2 2 2	36 32 31	0.8 0.9
5000	17 18 17	17 18 18	1 1 1	8 12 13	11 12 13	3 3 3	26 28 34	1.0 0.7
POSITIVE CONTROL 2-AA				274 277 399	317 317 317	71 71 71		19.4
10								
POSITIVE CONTROL MNNG	2450 1950 2050	2150 1950 2050	265 265 265				126.5	
5								

* : S-9 FRACTION/COFACTORS = 3:7 EXP : EXP TO 10

S. A. S. F. A. G.
DEPARTMENT OF TOXICOLOGY

AMES TEST WITH : 87/469
METHOD : STANDARD PLATE TEST

TABLE 2

STUDY NUMBER: 874072
STUDY DIREC.: ENC
OPERATOR: SCHL
DATE: 31.07.87

STRAIN: TA100

DOSE MCG/PL	REVERTANTS / PLATE				TITER DIL		QUOTIENT	
	-S9	M	SD	+S9*	M	SD	EXP-6	-S9
NEGATIVE CONTROL	104 118	114 104	9 106	113 106	108 108	5 5	41 53 48	1.0 1.0
DMSO	120							
20	108 112 119	113 117 115	6	109 117 115	114 114	4		1.0 1.1
100	124 126 134	128 116 126	5	113 116 126	118 118	7		1.1 1.1
500	98 97 100	98 110 96	2	121 110 96	109 109	13		0.9 1.0
2500	110 116 118	115 116 105	4	136 116 105	119 119	16	42 42 39	1.0 1.1
5000	115 132 115	121 123 124	10	114 123 124	120 120	6	32 37 34	1.1 1.1
POSITIVE CONTROL 2-AA				1890 1880 1950	1907 1907	38		17.7
	10							
POSITIVE CONTROL MNNG	2300 2250 2350	2300 2250 2350	50 50 50					20.2
	5							

* : S-9 FRACTION/COFACTORS = 3:7

EXP : EXP TO 10

S. A. S. F. A. G.
DEPARTMENT OF TOXICOLOGY

AMES TEST WITH : 87/469
METHOD : STANDARD PLATE TEST

TABLE : 3

STUDY NUMBER: 874072
STUDY DIREC.: ENT
OPERATOR : SCHU
DATE : 31.07.87
STRAIN: TA1537

DOSE MCG/PL	REVERTANTS / PLATE						TITER DIL	QUOTIENT	
	-S9	M	SD	+S9*	M	SD		EXP-6	-S9
NEGATIVE CONTROL	11 9	10	1	11 14	12	2	24 41	1.0	1.0
DMSO	10			10			37		
20	13 8 13	11	3	13 10 14	12	2		1.1	1.1
100	16 10 8	11	4	12 10 14	12	2		1.1	1.0
500	12 8 7	9	3	11 14 12	12	2		0.9	1.1
2500	8 7 13	9	3	11 12 15	13	2	32 29 38	0.9	1.1
5000	9 9 7	8	1	9 16 13	13	4	46 27 19	0.8	1.1
POSITIVE CONTROL Z-AA				369 383 399	384	15			32.9
10									
POSITIVE CONTROL AAC	1080 1140 1090	1103	32					110.3	
100									

* : S-9 FRACTION/COFACTORS = 3:7 EXP : EXP. TO 10

S. A. S. F. A.G.
DEPARTMENT OF TOXICOLOGY

TABLE 4

AMES TEST WITH : 87/469
METHOD : STANDARD PLATE TEST

STRAIN: TA98

STUDY NUMBER: 874072
STUDY DIREC.: ENC
OPERATOR : SCHW
DATE : 31.07.87

DOSE MCG/PL	REVERTANTS / PLATE						TITER DIL	QUOTIENT	
	-S9	M	SD	+S9*	M	SD		EXP-6	-S9
NEGATIVE CONTROL	21 22	22	1	31 30	31	2	58 62	1.0	1.0
DMSO	22			33			57		
20	25 21 16	21	5	30 41 37	36	6		1.0	1.1
100	19 17 16	17	2	36 29 31	32	4		0.8	1.0
500	14 15 13	14	1	33 33 29	32	2		0.6	1.0
2500	17 13 15	15	2	31 34 42	36	6	48 45 54	0.7	1.1
5000	12 15 11	13	2	32 30 34	32	2	27 18 23	0.6	1.0
POSITIVE CONTROL 2-AA				1420 1500 1450	1457	40			46.5
	10								
POSITIVE CONTROL NPO	757 738 712	736	23					34.0	
	10								

* : S-9 FRACTION/COFACTORS = 3:7

EXP : EXP. TO 10

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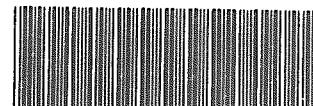
BASFBASF Aktiengesellschaft
D-6700 LudwigshafenSeite 1 von 2
Stand: 7/91

DIN - Sicherheitsdatenblatt

013831

Firma BASF Aktiengesellschaft

Handelsname PALATINOL® A

1.1 Chemische Charakterisierung:
Diethylphthalat

86940000391

1.2 Form : Fluessigkeit
1.4 Geruch: schwach

1.3 Farbe: farblos

2 Physikalische und sicherheitstechnische Angaben

geprueft nach

2.1	Zustandsanderung Pourpoint Siedebereich bei 5 mbar	-64 °C 175 - 182 °C °C °C °C	DIN ISO 3016
2.2	Dichte	(20 °C) 1,120 - 1,122 g/cm³ (°C) g/l (°C) kg/m³	DIN 51 757
2.3	Dampfdruck	(20 °C) 0,0044 mbar (°C) mbar	BASF
2.4	Viskosität	(20 °C) 12 - 14 mPa.s	DIN 53 015
2.5	Loeslichkeit in Wasser in	(20 °C) <0,1 g/l (°C) g/l	BASF
2.6	pH-Wert (bei g/l H₂O) (20 °C)		neutral
2.7	Flammpunkt		256 °C DIN 51 758
2.8	Zuendtemperatur		430 °C DIN 51 794
2.9	Explosionsgrenzen	untere: obere: Vol.% bei Normaltemperat. keine Expl.grenzen °C i.Anwendungsbereich	BASF
2.10	Thermische Zersetzung		
2.11	Gefahrliche Zersetzungprodukte:		
2.12	Gefahrliche Reaktionen:	Bei vorschrittsmaessiger Lagerung und Handhabung keine.	

2.13 Weitere Angaben: Temperaturklasse: T 2

DIN VDE 0165

3 Transport

CCVSee/IMDG-Code: keine
CCVE/CCVS : keineUN-NR. : keine
RID/ADR: keineICAO/IATA-DGR: keine
ADNR : keine

Sonstige Angaben:

4 Vorschriften

Palatinol A ist aufgrund uns vorliegender Daten kein gefahrlicher Stoff im Sinne von Anhang I Nr. 1.1 der GefStoffV bzw. des "EG-Leitfadens zur Einstufung und Kennzeichnung".

TA-Luft (Verwaltungsvorschrift zum Bundesimmissionsschutzgesetz - 28.02.1986): Kl. II (Moeglichkeit einer Zuordnung)

MAK-Wert (Bundesrepublik Deutschland 1986): nicht festgelegt

Handelsname PALATINOL® A**5 Schutzmassnahmen, Lagerung und Handhabung**

5.1 Technische Schutzmassnahmen: keine besonderen Massnahmen

5.2 Persoenliche Schutzausruestung:

Atemschutz:
Handschutz:Augenschutz: Schutzbrille
Andere :

5.3 Arbeitshygiene:

Beschmutzte, getraenkte Kleidung sofort ausziehen.

5.4 Brand- u. Explosionsschutz: Die beim Umgang mit Chemikalien ueblichen Massnahmen sind zu beachten

5.5 Entsorgung:

Kann unter Beachtung der oertlichen behoerlichen Vorschriften mit Hausmuell zusammen verbrannt werden.

6 Massnahmen bei Unfaellen und Braenden6.1 Nach Verschuetten/Auslaufen/Gasaustritt:
mit fluessigkeitsbindendem Material (z. B. Sand, Kieselgur, Sagemehl)
aufnehmen; s. 5.5

6.2 Loeschmittel:

Geeignete : Wasser, Wasserspruehstrahl, Loeschpulver, CO₂, Malone
Nicht zu verwenden:

6.3 Erste Hilfe:

Benetzte Kleidung entfernen

Haut: mit Wasser und Seife abspuelen

Augen: 15 Minuten bei gespreizten Lidern unter fliessendem Wasser
gruendlich ausspuelen

6.4 Weitere Angaben:

7 Angaben zur Toxikologie

Experimentelle Ergebnisse:

- LD 50 oral (Ratte): >9000 mg/kg
- primaere Hautreizwirkung (Kaninchen, OECD-Test): nicht reizend
- primaere Schleimhautreizwirkung (Kaninchen, OECD-Test): nicht reizend

8 Angaben zur Oekologie

Palatinol A sollte ohne Vorbehandlung nicht in Gewaesser gelangen.

Palatinol A ist durch mechanisches Abscheiden und biologischen Abbau
weitgehend aus dem Wasser eliminierbar.Bei sachgemaesser Einleitung geringer Konzentrationen in adaptierte
biologische Klaeranlagen sind keine Stoerungen der Abbauaktivitaet des
Belebtschlamm zu erwarten.**9.1 Weitere Hinweise**9.2 Die vorstehenden Angaben stuetzen sich auf den heutigen Stand unserer Kenntnisse und stellen kein
Zusicherung von Eigenschaften dar. Bestehende Gesetze und Bestimmungen sind vom Empfaenger unsere
Produkte in eignener Verantwortung zu beachten.

Sanitized Copy

CAS-No. 770-35-4

1-Phenoxy-2-propanol

COMPANY SANITIZED

- 1) Report on the study of acute oral toxicity of Solvenon PP (87/406, Nov. 24, 1987)
- 2) Study on the acute inhalation toxicity LC₅₀ of Protectol PP as a liquid aerosol in rats 4-hour exposure (90/634, Aug. 30, 1991)
- 3) Report on the acute dermal irritation/corrosivity to the intact dorsal skin of Protectol PP in white rabbits (90/634, Feb. 21, 1991)
- ✓4) Report on the study of the acute toxicity of Solvenon PP on Golden Orfe (87/406, Aug. 23, 1988)
- 5) Bestimmung des Verteilungskoeffizienten log Pow der Prüfsubstanz Protectol PP (J. Nr. 91P08243 vom 16.08.1991)
- 6) DIN Safety Data Sheet of Protectol PP (10/92)
- 7) Bestimmung der akuten Bakterientoxizität von Solvenon PP (J. Nr. 312021 vom 07.03.1989)
- 8) Solvenon PP: Prüfung von Substanzen für das Sicherheitsdatenblatt. Übersicht der Ergebnisse der Untersuchungen auf Eliminierbarkeit und Verhalten in Kläranlagen (10/1985)

~~904341~~

TEST FOR THE DETERMINATION OF THE INDEX OF OCULAR IRRITATION IN THE RABBIT

(following a method from "Code of Federal Regulations",
Title 16, Section 1500, 41)

1/ OBJECTIVE

This test is used to determine the degree of ocular irritation resulting from a test substance introduced into the conjunctival sac of the eye of the rabbit.

2/ EXPERIMENTAL PROTOCOL

2.1/ ANIMALS USED

Each test requires six male albino New Zealand white rabbits, weighing about 2.5 kg at the start of the trial. The animals will have been vaccinated against pasteurellosis and myxomatosis. Care is taken to select only those animals which have a normal eye condition, any with ocular lesions are rejected.

2.2/ HOUSING AND FEEDING

The rabbits are kept either in individual cages measuring 540 x 360 x 315 mm, or in restraining devices. The animal house is ventilated.^X The ear of each animal is pierced and a metal tag (Chevillot : La Quick) attached for individual identification.

200 g of food is provided per animal per day in the form of granules (Granulés Lepin "entretien" SANDERS). Water is provided ad libitum and automatically.

^X Renewal of air : 12 times per hour

- Hygrometry = 55% ± 20 (Controlled with an Hygrometer-Thermometer)

2.3/ DOSE AND ADMINISTRATION OF TEST SUBSTANCE

(amount deposited into the conjunctival sac of the eye = 0,1 ml)*

- Substance tested UNDILUTED, without rinsing.

2.4/ METHOD OF ADMINISTRATION OF TEST PRODUCT

Each animal is immobilised in a restraining box. The test substance is then introduced into the animal's right eye, the animal's left eye serves as a control. The eye lids are held closed for several seconds, moved gently up and down and avoiding loss of the substance. The animals are kept restrained for 18 hours and then placed in their cages.

2.5/ READING THE SITE OF OCULAR IRRITATION

To make a reading of the site of ocular irritation, the animals are placed in restraining boxes. Evaluations are made by comparison with the control eye. The readings are made 1 hour after the administration of the test substance, then at 24 hours after administration, 2 days, 3 days, 4 days, and 7 days after administration. When the irritation is persistent, readings are made each week over a maximum period of 2 weeks. If the lesions are too important and prevent the ocular observations or if the intensity of the lesions increases after D 7, the animals are sacrificed and the eye examined macroscopically. Observations of the condition of the cornea are made with the naked eye and also with the aid of an ophthalmoscope of Heine (Miriflex C-00.13.101). The ophthalmoscope may also be used to observe the iris, pupil and lens. A supplementary examination may be performed with a slit lamp (Haag-Streit).

3/ EVALUATION OF OCULAR IRRITATION

3.1/ CONJUNCTIVAL LESIONS AND DISCHARGE

An alteration of the palpebral conjunctiva is minor compared with corneal opacification or a lesion of the iris and pupil.

The anomalies found in the conjunctiva are scored according to the following scale :

CHEMOSIS (oedema) - A -

- | | |
|---|---|
| - No swelling..... | 0 |
| - Slight swelling (including nictitating membrane)..... | 1 |
| - Obvious swelling with partial eversion of lids..... | 2 |
| - Swelling with lids up to half closed..... | 3 |
| - Swelling with lids more than half closed..... | 4 |

DISCHARGE - B -

- | | |
|---|---|
| - Absence of discharge..... | 0 |
| - Discharge slight (does not include the small amount normally found in inner canthus)..... | 1 |
| - Discharge with moistening of lids and hairs adjacent to lids..... | 2 |
| - Discharge with moistening of lids and a considerable area around the eye..... | 3 |

Note : The evaluation of discharge and swelling should be conducted before opening the lids of the animals.

CONJUNCTIVAL ENANTHEMA (visible by pulling open the eye lids) - C -

- | | |
|---|---|
| - Vessels normal..... | 0 |
| - Vessels definitely congested above normal..... | 1 |
| - More diffuse, deeper crimson red, individual vessels not discernable..... | 2 |
| - Diffuse beefy red..... | 3 |

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3.2/ PUPILLARY AND IRIDIAL LESIONSPUPIL

The dimension, form and position of the pupil is compared with the control eye. The pupillary direct photomotor reflex (contraction of iris to reduce pupil size) is observed by shining a bright light into the eye.

IRIS

The iris is examined with direct lighting and then lighting from the side. The colour, uniformity and texture are observed.

Alterations in pupil or iris are scored using the following scale :

- No anomaly..... 0
- Iris clearly more folded than normal, congestion, swelling, circumcorneal injection (any one or all of these), iris still reacting to light (sluggish reaction is positive)..... 1
- No reaction to light, haemorrhage ; gross destruction (any one or all of these)..... 2

Note : the total score is multiplied by 5 (maximum possible : 10)

3.3/ CORNEAL LESIONS

The cornea is normally glossy, transparent and without visible blood vessels.

(§) Quantitative evaluations of the DEGREE AND EXTENT OF OPACITY of the cornea are scored according to the following system.

(§) To determine the presence or absence of corneal opacification and to evaluate the extent of surface attack a 2% solution of fluorescein (CHIBRET) is instilled into the eye. Excess fluorescein is rinsed away with a jet of rinsing solution (DACYROSERUM - Chibret).

So that the results are not affected this method, which requires a rinse, is not conducted until after the reading made 1 hour after the instillation of the test substance.

Rinsing solution : when the details of the nature of the test substance are not known, the following solution is used as a rinsing agent : DACYROSERUM (CHIBRET Laboratories - France)
..... Serric acid 1/8 g

- Degree of opacity (A)

(the most opaque area is chosen for the reading)

- No opacity. Neither loss of brilliance nor gloss..... 0
- Opacity scattered or diffuse, details of iris clearly visible..... 1
- Translucent zone easily discernable, details of iris slightly obscured..... 2
- Opalescent zone, no details of iris visible, size of pupil barely discernable..... 3
- Cornea completely opaque, iris invisible..... 4

- Area of cornea affected (B)

- One quarter (or less) but not zero..... 1
- Greater than one quarter, up to one half 2
- Greater than one half, up to three quarters 3
- Greater than three quarters, up to whole area..... 4

Note : the total score is obtained by applying the formula :

$$A \times B \times 5 \text{ (maximum total : 80)}$$

A qualitative evaluation of any ULCERATION or GRANULATION of the cornea is conducted to determine the irritative capacity of the test substance :

- Ulceration (loss of substance with or without swelling of the eye)

- No ulceration..... 0
- Presence of ulceration..... U

- Area affected

- . One quarter (or less) but not zero a
- . Greater than one quarter, up to one half b
- . Greater than one half, up to three quarters c
- . From three quarters to total area d

Note : the best method for demonstrating the nature and degree of this lesion is the fluorescein test.

- Granulous dystrophy (multiple blisters spread over the corneal epithelium)

- . No granulation 0
- . Presence of granulation G

- Area affected

- . One quarter (or less) but not zero a
- . Greater than one quarter, up to one half b
- . Greater than one half, up to three quarters c
- . From three quarters to total area d

4/ INTERPRETATION OF RESULTS

The total number of eye lesions found in the conjunctiva, iris and cornea of each animal allows the calculation of the Individual Index of Ocular Irritation (I.I.O.I.) at each of the different observation times (1 hour and 1, 2, 3, 4 & 7 days after the instillation of the test substance).

A mean score per zone (conjunctiva, iris and cornea) is also calculated for the total of treated animals at 1 hour and 1, 2, 3, 4 & 7 days.

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The mean of the individual index of ocular irritation (I.I.O.I.) obtained at each observation time for the 6 rabbits treated allows the calculation of the "Mean Index of Ocular Irritation" (M.I.O.I.) and standard deviation and also to see the dispersion of the values within each group at different times.

The mean Indexes of Ocular Irritation (M.I.O.I.) obtained from readings at D 1, D 2 and D 3 are added and the sum is divided by 3.

This score enables the test substance to be classified, according to BASF specifications.

Classification of test substance

From 0 up to 10	NON IRRITANT
From 11 up to 25	SLIGHTLY IRRITANT
From 26 up to 56	MODERATELY IRRITANT
From 57 up to 110	STRONGLY IRRITANT

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R E S U L T S

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OCULAR IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE: 78/531 = Corialmattierung G

APPLICATION: 0.1 ml per animal of undiluted reference substance (without rinsing)DATE OF INSTILLATION: MARCH, 13th 1979

EVALUATION OF EFFECTS:		I H					D 1					D 2								
N° of rabbits :		648	649	650	651	652	653	648	649	650	651	652	653	648	649	650	651	652	653	
CONJUNCTIVA	A) Chaemosis	0-4	2	1	1	2	2	1	3	4	3	3	3	2	3	3	4	3	2	3
	B) Discharge	0-3	1	2	1	1	1	1	2	2	2	2	2	1	2	1	2	2	2	2
	C) Enanthemea	0-3	1	1	1	1	1	1	2	2	2	2	2	1	1	2	2	2	2	2
	(A + B + C) X 2 (max. = 20)		8	8	6	8	8	6	14	16	14	14	12	10	10	14	16	14	12	14

DIRECT PHOTOMOTOR REFLEX OF PUPIL (\$)		N	N*	N*	N*	N*	N	N*											
IRIS	Congestion	0-2	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°	1°
	X 5 (max. = 10)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

(\$ N = Normal

- R = Reduced

- No reflex

CORNEA	A) Opacity	0-4	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	B) area affected)	1-4	4	1	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	A X B X 5 (max. = 80)	40	10	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40
ULCERATION		U	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Area affected		a-d	a	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
GRANULATION		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Area affected		a-d	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Individual ocular irritation score IOI	53	23	51	53	53	51	59	61	59	59	57	55	55	59	61	59	57	59
(max. : 110)																		

OBSERVATIONS:

- Circumcorneal injection + congestion of the iris
- * Permanent myosis with preservation of direct photomotor reflex.

MEAN SCORE PER ZONE	Conj. + Iris + Corn.	Conj. + Iris + Corn.	Conj. + Iris + Corn.
	7.22	5.00	25.00

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OCULAR IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE: 78/531 = Corialmattierung G

APPLICATION: 0.1 ml per animal of undiluted reference substance (without rinsing)DATE OF INSTILLATION: MARCH, 13th 1979

EVALUATION OF EFFECTS:		D.3					D.4					D.7								
N° of rabbits :		648	649	650	651	652	653	648	649	650	651	652	653	648	649	650	651	652	653	
CONJUNCTIVA	A) Chaemosis	0 - 4	3	2	3	3	2	4	2	2	3	3	2	4	2	2	1	2	2	4
	B) Discharge	0 - 3	1	1	2	2	2	2	1	1	2	2	1	2	0	0	0	1	1	2
	C) Enanthemea	0 - 3	1	2	2	2	2	2	1	2	2	2	2	3	1	1	1	2	2	3
	(A + B + C) X 2 (max. = 20)	10	10	14	14	12	16	8	10	14	14	10	18	6	6	4	10	10	18	

DIRECT PHOTOMOTOR REFLEX OF PUPIL (§)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
IRIS	Congestion	0 - 2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	X 5 (max. = 10)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

(§) N = Normal

- R = Reduced

- No reflex

CORNEA	A) Opacity	0 - 4	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	
	B) area affected)	1 - 4	4	4	3	4	4	4	4	4	4	3	3	4	4	3	2	3	4
	A X B X 5 (max. = 80)	40	40	30	40	40	40	40	40	30	30	40	40	30	20	30	30	40	
	ULCERATION	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Area affected		a - d	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	
GRANULATION		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Area affected		a - d	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	

Individual ocular irritation score 101 (max. : 110) 55 55 49 59 57 61 53 55 49 49 55 63 41 31 39 45 55 63

OBSERVATIONS :

- * Permanent myosis with preservation of direct photomotor reflex.
- ° Circumcorneal injection + congestion of the iris
- x Revascularization zone well defined

MEAN SCORE PER ZONE	Conj. + Iris	+ Corn.	Conj. + Iris	+ Corn.	Conj. + Iris	+ Corn.
	12.67	5.00	38.33	12.33	5.00	36.67

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OCULAR IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE: 78/531 = Corialmattierung G

APPLICATION: 0.1 ml per animal of undiluted reference substance (without rinsing)DATE OF INSTILLATION: MARCH, 13th 1979

EVALUATION OF EFFECTS:		D 14					D 21							
N° of rabbits :		648	649	650	651	652	653	648	649	650	651	652	653	
CONJUNCTIVA	A) Chaemosis	0 - 4	2	2	2	2	2	4	2	2	2	2	2	4
	B) Discharge	0 - 3	0	0	2	0	1	2	0	0	0	0	1	2
	C) Enantherma	0 - 3	1	1	2	1	1	2	1	1	1	1	1	2
	(A + B + C) X 2 (max. = 20)		6	6	12	6	8	16	6	6	6	6	8	16

DIRECT PHOTOMOTOR REFLEX OF PUPIL (\$)		N	N	N	N	N	N	N	N	N	N	N	R	
IRIS	Congestion	0 - 2	1	1	1	1	1	1	1	1	1	1	1	
	X 5 (max. = 10)		5	5	5	5	5	5	5	5	5	5	5	

(\$) N = Normal - R = Reduced - No reflex

CORNEA	A) Opacity	0 - 4	2 ^x	2 ^x	2 ^x	2 ^x	3 ^x	2 ^x						
	B) area affected	1 - 4	2	2	2	2	2	2	2	2	2	2	2	1
	A X B X C (max. = 80)		20	20	20	20	30	20	20	20	20	20	20	
	ULCERATION		0	0	0	0	0	0	0	0	0	0	0	
	Area affected	a - d	/	/	/	/	/	/	/	/	/	/	/	
	GRANULATION		0	0	0	0	0	0	0	0	0	0	0	
	Area affected	a - d	/	/	/	/	/	/	/	/	/	/	/	

Individual ocular irritation score IOI (max. : 110)	31	31	37	31	43	41	31	31	31	31	33	41		
--	----	----	----	----	----	----	----	----	----	----	----	----	--	--

OBSERVATIONS:

- * Permanent myosis with preservation of direct photomotor reflex.
- ° Circumcorneal injection + congestion of the iris
- Revascularization zone well defined

MEAN SCORE PER ZONE	Conj. + Iris + Corn.	Conj. + Iris + Corn.	Conj. + Iris + Corn.
	9.00 5.00 21.67	8.00 5.00 20.00	

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6/ CONCLUSION

=====

The results found under the experimental conditions of this study
are used to classify the test substance :

78/531 = Corialmattierung G

following the scale mentioned above (B.A.S.F.)

	TIME ELAPSED AFTER INSTILLATION							
	1 hour	Day 1	Day 2	Day 3	Day 4	Day 7	Day 14	Day 21
TEST SUBSTANCE APPLIED UNDILUTED (WITHOUT RINSING)	47.3	58.3	58.3	56.0	54.0	45.7	35.7	33.0

The sum of Mean Indexes of Ocular Irritation (M.I.O.I.) obtained
at 24, 48 and 72 hours = $58.3 + 58.3 + 56.0 = 172.6$

IRRITATION SCORE = $172.6 / 3 = 57.5$

STRONGLY IRRITANT APPLICATION

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DETERMINATION OF THE INDEX
OF PRIMARY CUTANEOUS IRRITATION
IN THE RABBIT

TEST FOR THE DETERMINATION OF THE INDEX
OF PRIMARY CUTANEOUS IRRITATION IN THE RABBIT

(following a method from "Code of Federal Regulations,
Title 16, Section 1500.42)

1/ OBJECTIVE

=====

This method is used to determine the primary irritation resulting from the application of a test substance. Primary irritants are those substances which, with a single application, cause an inflammatory cutaneous orthoergic reaction. The reaction is localised at the point of contact and appears within 24 hours of application.

The irritation depends upon the test substance, its concentration and the length of time it remains in contact with the skin.

2/ EXPERIMENTAL PROTOCOL

=====

2.1/ EXPERIMENTAL ANIMALS

Six male albino New Zealand white rabbits are used for each trial. They weigh between 2.5 kg and 3.5 kg at the start of the test, and they will have been vaccinated against pasteurellosis and myxomatosis. Only healthy animals without signs of skin lesions are selected for use.

2.2/ MAINTENANCE OF ANIMALS

The rabbits are kept in individual cages measuring 540 X 360 X 315 mm or in restraining devices which allow the back of the animal to be treated. The animal house is ventilated*. The ear of each animal is pierced and a metal tag (Chevillot : La Quick) attached for individual identification.

* Renewal of air = 12 times per hour

- Hygrometry = 55% ± 2% {Controlled with an Hygrometer-Thermometer :

200 g of food is provided per animal per day in the form of granules (Granulés Lapin "entretien" SANDERS). Water is given automatically and ad libitum.

2.3/ TEST METHOD

2.31/ PREPARATION OF THE SKIN

The six rabbits are clipped with a fine toothed electric clipper (AESCLAP - Type V 42 947) to bare a skin surface of 14 cm X 14 cm (The cutting height = 1/20e mm) ; thus a precise cut can be achieved without irritating the skin mechanically. The animals are left to rest for 24 hours and then only those with perfectly healthy skin are chosen for the test.

The right flank is scarified with a sterile scalpel blade, making three parallel superficial incisions 2 cm long and 0.5 cm apart. The incisions are epidermal and do not damage the dermis (should bleeding occur, a fresh animal is utilised).

2.32/ APPLICATION OF THE TEST SUBSTANCE

The compound¹ to be tested is applied to the rabbit skin, using the right, previously scarified flank and the left intact one, at a rate of 0.5 ml² per area and animal in the case of a viscous compound and at 0.5 g³ per area and animal when dealing with a powdery or pasty material (solid material -powder- is applied in paste form). These treated areas are subsequently covered with a 2 cm square gauze pad consisting of sterile, hydrophilic gauze of four layers. The material to be tested and the gauze pads are kept in contact with the skin by a patch⁴ (NEODERMOTEST ROC) consisting of a central, circular disc of 22 mm diameter with a surrounding adhesive, hypoallergenic, perforated plaster 10 mm wide.

¹ Product administered in its pure, undiluted form

² The volume of the product is measured and applied with a sterile, polypropylene syringe (Becton Dickinson) of 2.5 ml

³ Weighing done with a METTLER balance - type PL 200 ($d = 1$ mg)
and the material kept in a haemolysis tube.

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Finally, an adhesive tape 6 cm wide is wound around the animal to complete the fixing of the patches. Care is taken so that the respiratory and abdominal movements of the animal are not restricted.

The rabbits are then placed for 24 hours in restraining devices.

2.4/ EVALUATION OF PRIMARY CUTANEOUS IRRITATION

After 24 hours of contact with the skin, the patches are removed. One hour later, the primary irritation index is evaluated and the animals are then put back into their individual cages. 48 hours later, a second reading is made to determine the extent of any recovery (the two readings are performed respectively 25 and 72 hours after the application of the substance).

If after the last reading, any irritation is noted, the animals are maintained under observation for one week. On the 7th day, another reading is made, special attention to be paid to the presence of desquamation at the site of application.

Readings are made of both the scarified and non scarified zones, following the scale of scores proposed by the "Journal Officiel", as shown below :

Erythematous (and scar) lesions

- No erythema..... 0
- Very slight erythema (barely perceptible)..... 1
- Well defined erythema..... 2
- Moderate to severe erythema..... 3
- Severe erythema, crimson red, with slight eschar formation (injuries in depth)..... 4

Oedematous lesions

- No oedema..... 0
- Very slight oedema (barely perceptible)..... 1
- Slight oedema (edges of area well defined by definite raising)..... 2
- Moderate oedema (area raised approximately 1 mm)..... 3

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2.5/ SCORING

The scores obtained on the normal and abraded zones of each animal, for erythema and oedema respectively, are added at 25 and 72 hours.

Each of the 8 total scores are divided by 6 (number of rabbits per test) or by the number of animals for which a reading was possible.

A mean value at a given time (25 and 72 hours) is thus obtained for each reading. These means are added for erythema (ΣE) and for oedema (ΣO).

The sum of the erythema means (ΣE) and that of the oedema (ΣO) is divided by 4 ($\Sigma E + \Sigma O$) ; the figure obtained (never above 8) represents the Primary Cutaneous ⁴ Irritation Index.

This index allows to classify the test substance as follows :

<u>Index of primary irritation</u>	<u>Classification of the test material</u>
From 0.0 up to 0.5	NON-IRRITANT
From 0.6 up to 3.0	SLIGHTLY IRRITANT
From 3.1 up to 5.0	MODERATELY IRRITANT
From 5.1 up to 8.0	SEVERELY IRRITANT

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R E S U L T S

PRIMARY CUTANEOUS IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE: 78/531 = Corialmattierung G

APPLICATION: 0.5 ml per zone, per animal of undiluted reference substanceDATE OF APPLICATION: MARCH, 20th 1979

RABBITS N°		937	938	939	940	941	942	TOTAL	MEAN
ERYTHEMA	NORMAL	25 h.	2	0	2	2	2	1	1.5
	SCARIFIED	72 h.	3	0	3	3	3	2	2.3
	SCARIFIED	7 d.	SS	§	SS	SS	SS	SS	
OEDEMA	NORMAL	25 h.	1	1	2	2	2	2	1.7
	SCARIFIED	72 h.	2	0	3	2	3	2	2.0
	SCARIFIED	7 d.	SS	§	SS	SS	SS	SS	ΣE 7.5

RABBITS N°		937	938	939	940	941	942	TOTAL	MEAN
OEDEMA	NORMAL	25 h.	1	0	0	0	1	0	0.3
	SCARIFIED	72 h.	1	0	1	1	2	2	1.2
	SCARIFIED	7 d.	1	§	0	0	1	1	
IRRITATION	NORMAL	25 h.	0	0	0	0	1	0	0.2
	SCARIFIED	72 h.	1	0	1	1	1	1	0.8
	SCARIFIED	7 d.	0	§	0	0	0	0	ΣO 2.5

OBSERVATIONS:

SS = Important desquamation

§ = Rabbit N° 938 died on MARCH, 23th 1979
(after observation) and was not replaced.PRIMARY CUTANEOUS IRRITATION SCORE $(\frac{\Sigma E + \Sigma O}{4})$

SAMPLE CLASSIFICATION

Non-irritant : 0.0 - 0.5

Slightly Irritant : 0.6 - 1.0

Moderately Irritant : 1.1 - 2.0

Strongly Irritant : 2.1 - 4.0

Substanz: Corialverdünner EB
Substanz-Nr.: 77/930

ERGEBNIS DER GEWERBETOXIKOLOGISCHEN GRUNDPRÜFUNG

1. AKUTE ORALE TOXIZITÄT (Ratte):

$LD_{50} > 5000$ mg/kg.

2. AKUTES INHALATIONSRISIKO (3):

Akutes Inhalationsrisiko (Ratte; abhängig von Toxizität UND Flüchtigkeit; Rückschlüsse auf die akute Inhalationstoxizität sind nicht möglich):

Nach 30 Minuten Exposition in einer bei 20 °C angereicherten Atmosphäre keine Tiere gestorben. Todesfälle nach längerer Exposition. Im Versuch wurden Reizerscheinungen an Augen und Atemorganen beobachtet.

Aufgrund der Befunde besteht eine Gefährdung beim Einatmen der flüchtigen Anteile.

Es ist zu berücksichtigen, daß die Ergebnisse des Inhalationsrisikotestes eine Gefahr kennzeichnen, die durch die hohe Flüchtigkeit der Substanz bedingt sein kann. Rückschlüsse auf eine akute Giftigkeit (Inhalationstoxizität) sind aufgrund dieses Testes allein nicht möglich.

3. PRIMÄRE HAUTREIZWIRKUNG (geprüft am Kaninchen nach (6)):

Primärer Reizwert: 0,2 (vgl. 6)

Aufgrund der Befunde muß die Substanz als NICHT REIZEND bezeichnet werden.

Leichte Reizerscheinungen wurden nur an der skarifizierten Haut beobachtet.

Sie bildeten sich innerhalb von 7 Tagen zurück.

4. PRIMÄRE SCHLEIMHAUTREIZWIRKUNG (geprüft am Kaninchenauge nach (6)):

Primärer Reizwert: 9,7 (vgl. 6)

Aufgrund der Befunde muß die Substanz als NICHT REIZEND bezeichnet werden.

Bei Einwirkung der Substanz auf die Augen können leichte reversible HORNHAUTTRÜBUNGEN und ENTZÜNDUNGEN AN DER REGENBOGENHAUT

Substanz: Corialverdünner EB
Substanz-Nr.: 77/930

Die pathologischen Befunde am Auge und die leichten Reizerscheinungen an der Schleimhaut bildeten sich innerhalb von 7 Tagen zurück.

S I C H E R H E I T S R A T S C H L Ä G E :

Einatmen eines angereicherten Dampf/Luftgemisches vermeiden.

Im übrigen sind die beim Umgang mit Chemikalien allgemein üblichen Vorsichtsmaßregeln zu beachten.

B E S O N D E R E B E M E R K U N G E N :

AKUTE INTRAPERITONEALE TOXIZITÄT (Maus): LD₅₀ > 700 und < 2000 mg/kg.

Äthylacetat, Butylacetat, Äthylglykolacetat sind in der EG-Liste zur Kennzeichnung gefährlicher Stoffe, in der Arbeitsstoff-Verordnung und in der MAK-Liste aufgeführt. Die sich hieraus ergebenden Konsequenzen sind zu beachten.

a) Vorschlag für die ZUORDNUNG VON R- UND S-SÄTZEN (Amtsblatt der EG, 30.12.76, 76/907/EWG):

R: 37 = Reizt die Atmungsorgane

S: 23 = Gas/Rauch/Dampf/Aerosol nicht einatmen

b) Vorschlag zum Gefahrensymbol: Xi = reizend

Die Zuordnung der R- und S-Sätze sowie des Gefahrensymbols stützt sich allein auf die Haut- und Schleimhautreizwirkung und die orale und mit Einschränkung die inhalatorische Toxizität.

(3) In Anlehnung an H.F. Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107 (1962)

(6) Federal Register 38 No 187 § 1500.41 (Haut) und § 1500.42 (Auge), S. 27019 vom 27.09.73.

Bewertung nach: Draize, J.H. (1959): Dermal Toxicity. In: FDA-Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics.


Dr. med. H. Zeller


Dr. med. habil. Dr. rer. nat. Gelbke

AKUTE TOXIZITAET

DOSIS	MG/KG	I	5000	I	2150	I
		I		I		I

MORTALITAET:

	M	I		M	I
ANZAHL DER TIERE	I	5	I	5	I
	I				
TOTE TIERE NACH	I				
1 H I		0	I	0	I
1 D I		0	I	0	I
2 D I		0	I	0	I
7 D I		0	I	0	I
14 D I		0	I	0	I

	W	I		W	I
ANZAHL DER TIERE	I	5	I	5	I
	I				
TOTE TIERE NACH	I				
1 H I		0	I	0	I
1 D I		0	I	0	I
2 D I		0	I	0	I
7 D I		0	I	0	I
14 D I		0	I	0	I

MITTELGEW. (G):

	M	I		M	I
VERSUCHSBEGINN	I	180	I	210	I
	I				
NACH:	I				
2- 4D I	218		I	228	I
7 D I	232		I	264	I
13 D I	270		I	286	I

	W	I		W	I
VERSUCHSBEGINN	I	150	I	170	I
	I				
NACH:	I				
2- 4D I	175		I	191	I
7 D I	180		I	196	I
13 D I	193		I	201	I

SYMBOLE : D = "TAG" ; H = "STUNDE"
 M = MAENNLICH ; W = WEIBLICH

77 / 930 MAUS / I.P.

BLATT 1

AKUTE TOXIZITAET
=====

SUBSTANZ NUMMER I 77 / 930
 SUBSTANZBEZ. I CORIALVERDUENNER EB
 ZUBEREITUNG MIT I 0.5% WAESS. CARBOXYMETHYLCELLULOSE ZUBER.
 APPLIKATIONSFORM I EMULSION
 APPLIKATIONSART I INTRAPERITONEAL
 TIERART I MAUS/NMRI/WIGA
 FUTTER I HERILAN MRH-HALTUNG; H. EGGERSMANN KG
 NUECHTERNPERIODE I 15H - 20H VOR APPL.
 BEOBUCHTUNGSDAUER I 14 D
 DATUM ERSTE APPL. I 14. 4. 78
 DATUM LETZTE APPL. I 18. 5. 78

DOSIS	MG/KG	I	2000	I	700	I
KONZ. %	(G/V)	I	20	I	7	I
APPL. VOL.	ML/KG	I	10	I	10	I

ERGEBNIS

LD50 NACH 14 D

M+W : GROESSER 700 (MG/KG) (1 % SIGNIFIKANZLEVEL)
 KLEINER 2000 (MG/KG) (1 % SIGNIFIKANZLEVEL)

VERSUCHSDURCHFUEHRUNG : DR. MED. HABIL. DR. RER. NAT. H.-P. GELEKE



SYMBOLE : D = "TAG" ; H = "STUNDE"
 M = MAENNLICH ; W = WEIBLICH

AKUTE TOXIZITAET
=====

DOSIS	MG/KG	I	2000	I	700	I
		I		I		I

MORTALITAET:

	M	I				
ANZAHL DER TIERE	I	5	I	5	I	
	I					
TOTE TIERE NACH	I					
1 H I		5	I	0	I	
1 D I		5	I	0	I	
2 D I		5	I	0	I	
7 D I		5	I	0	I	
14 D I		5	I	0	I	

	W	I				
ANZAHL DER TIERE	I	5	I	5	I	
	I					
TOTE TIERE NACH	I					
1 H I		5	I	0	I	
1 D I		5	I	0	I	
2 D I		5	I	0	I	
7 D I		5	I	0	I	
14 D I		5	I	0	I	

MITTELGEW. (G):

	M	I				
VERSUCHSBEGINN	I	30	I	28	I	
	I					
NACH:	I					
2- 4D I			I	29.2	I	
7 D I			I	31.2	I	
13 D I			I	33.6	I	

	W	I				
VERSUCHSBEGINN	I	24	I	24	I	
	I					
NACH:	I					
2- 4D I			I	25.1	I	
7 D I			I	25.4	I	
13 D I			I	27.6	I	

SYMBOLE : D = "TAG" ; H = "STUNDE"
M = MAENNLICH ; W = WEIBLICH

17 17 4 17

Substanz: Corialverdünner EB
Substanz-Nr.: 77/930

AKUTES INHALATIONSRISIKO - Inhalations-Risiko-Test (Ratte) *

Inhalation einer mit Dampf flüchtigen Anteilen bei 20 °C
angereicherten Atmosphäre. Es werden zur Anreicherung 200 l Luft/h durch eine 5 cm hohe Schicht des Produktes geleitet.

Mortalität x/y gestorbene/exponierte Tiere

Expositionszeit	3'	10'	30'	1 h	3 h	7 h
Dampf						
flüchtige Anteile			0/12	3/6		
Staub						

SYMPTOME:

Fluchtversuche, wässriges Augen- und Nasensekret, Schnappatmung, verminderte Schmerzreaktion, stark taumelnder Gang, Seitenlage, Narkose.

Klimisch

.....
Dr.rer.nat.Klimisch

SEKTIONSBEFUNDE:

.....
Dr.med.vet.Freisberg



IFREB

Institut Français de Recherches et Essais Biologiques

77/930 : CORIALVERDÜNNER EB

B . A . S . F

LOCAL TOLERANCE TESTS IN THE RABBIT

- INDEX OF OCULAR IRRITATION
- INDEX OF PRIMARY CUTANEOUS IRRITATION



IFREB

Institut Français de Recherches et Essais Biologiques

Centre de Lyon / Les Oncins

IFREB - R

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SPECIMEN N°

77/930 : CORIALVERDÜNNER EB

B.A.S.F

LOCAL TOLERANCE TESTS IN THE RABBIT

- INDEX OF OCULAR IRRITATION
- INDEX OF PRIMARY CUTANEOUS IRRITATION

ST-GERMAIN-SUR-L'ARBRESLE,
DECEMBER 12th, 1978

19.1.79 f

INSTITUT FRANÇAIS DE RECHERCHES
ET ESSAIS BIOLOGIQUES

001

Centre de LYON - LES ONCINS
B.P. 109 - 69210 L'ARBRESLE
FRANCE

FIRM

B. A. S. F

TEST SUBSTANCE

77/930 : Corialverdünner EB

S - LOCAL TOLERANCE TESTS IN THE RABBIT

=====

(Following a method from "Code of
Federal Regulations" Title 16,
Sections 1500, 41 and 42)

- INDEX OF OCULAR IRRITATION

Substance tested undiluted,

no rinse = 9.7

NON-IRRITANT

- INDEX OF PRIMARY CUTANEOUS IRRITATION

Substance tested undiluted .. = 0.2

NON-IRRITANT



B. COQUET

Docteur en Pharmacie
Licencié ès Sciences



J.P. GUILLOT

Responsable de l'Etude
Chef du Service

11 4 5

INTRODUCTION

Upon request from B.A.S.F the tests described below were carried out on the following :

77/930 : Corialverdünner EB

- DETERMINATION OF THE INDEX OF OCULAR IRRITATION,
in the rabbit.

(p. 3 to 14)

- DETERMINATION OF THE INDEX OF PRIMARY CUTANEOUS IRRITATION,
in the rabbit.

(p. 15 to 21)

I.F.R.E.B.-R

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003

DETERMINATION OF THE INDEX
OF OCULAR IRRITATION
IN THE RABBIT

TEST FOR THE DETERMINATION OF THE INDEX OF OCULAR IRRITATION IN THE RABBIT

(following a method from "Code of Federal Regulations",
Title 16, Section 1500, 41)

1/ OBJECTIVE

=====

This test is used to determine the degree of ocular irritation resulting from a test substance introduced into the conjunctival sac of the eye of the rabbit.

2/ EXPERIMENTAL PROTOCOL

=====

2.1/ ANIMALS USED

Each test requires six male albino New Zealand white rabbits, weighing about 2.5 kg at the start of the trial. The animals will have been vaccinated against pasteurellosis and myxomatosis. Care is taken to select only those animals which have a normal eye condition, any with ocular lesions are rejected.

2.2/ HOUSING AND FEEDING

The rabbits are kept either in individual cages measuring 540 x 360 x 315 mm, or in restraining devices. The animal house is ventilated. The ear of each animal is pierced and a metal tag (Chevilllet : La Quick) attached for individual identification.

200 g of food is provided per animal per day in the form of granules (Granulés Lepin "entretien" SANDERS). Water is provided ad libitum and automatically.

2.3/ DOSE AND ADMINISTRATION OF TEST SUBSTANCE

(amount deposited into the conjunctival sac of the eye = 0,1 ml)^{*}

- Substance tested UNDILUTED, without rinsing.

2.4/ METHOD OF ADMINISTRATION OF TEST PRODUCT

Each animal is immobilised in a restraining box. The test substance is then introduced into the animal's right eye, the animal's left eye serves as a control. The eye lids are held closed for several seconds, moved gently up and down and avoiding loss of the substance. The animals are kept restrained for 18 hours and then placed in their cages.

2.5/ READING THE SITE OF OCULAR IRRITATION

To make a reading of the site of ocular irritation, the animals are placed in restraining boxes. Evaluations are made by comparison with the control eye. The readings are made 1 hour after the administration of the test substance, then at 24 hours after administration, 2 days, 3 days, 4 days, and 7 days after administration. When the irritation is persistent, readings are made each week over a maximum period of 2 weeks. If the lesions are too important and prevent the ocular observations or if the intensity of the lesions increases after D 7, the animals are sacrificed and the eye examined macroscopically. Observations of the condition of the cornea are made with the naked eye and also with the aid of an ophthalmoscope of Heine (Miriflex C-00.13.101). The ophthalmoscope may also be used to observe the iris, pupil and lens. A supplementary examination may be performed with a slit lamp (Haag-Streit).

* The volume of the product is measured and instilled with a sterile

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3/ EVALUATION OF OCULAR IRRITATION

3.1/ CONJUNCTIVAL LESIONS AND DISCHARGE

An alteration of the palpebral conjunctiva is minor compared with corneal opacification or a lesion of the iris and pupil.

The anomalies found in the conjunctiva are scored according to the following scale :

CHEMOSIS (oedema) - A -

- No swelling..... 0
- Slight swelling (including nictitating membrane)..... 1
- Obvious swelling with partial eversion of lids..... 2
- Swelling with lids up to half closed..... 3
- Swelling with lids more than half closed..... 4

DISCHARGE - B -

- Absence of discharge..... 0
- Discharge slight (does not include the small amount normally found in inner canthus)..... 1
- Discharge with moistening of lids and hairs adjacent to lids..... 2
- Discharge with moistening of lids and a considerable area around the eye..... 3

Note : The evaluation of discharge and swelling should be conducted before opening the lids of the animals.

CONJUNCTIVAL ENANTHEMA (visible by pulling open the eye lids) - C -

- Vessels normal..... 0
- Vessels definitely congested above normal..... 1
- More diffuse, deeper crimson red, individual vessels not discernable..... 2
- Diffuse beefy red..... 3

Note : For the total score, the three values are added and multiplied by 2. (A+B+C) X 2 (maximum score : 20)

3.2/ PUPILLARY AND IRIDIAL LESIONS

PUPIL

The dimension, form and position of the pupil is compared with the control eye. The pupillary direct photomotor reflex (contraction of iris to reduce pupil size) is observed by shining a bright light into the eye.

IRIS

The iris is examined with direct lighting and then lighting from the side. The colour, uniformity and texture are observed.

Alterations in pupil or iris are scored using the following scale :

- No anomaly..... 0
- Iris clearly more folded than normal, congestion, swelling, circumcorneal injection (any one or all of these), iris still reacting to light (sluggish reaction is positive)..... 1
- No reaction to light, haemorrhage : gross destruction (any one or all of these)..... 2

Note : the total score is multiplied by 5 (maximum possible : 10)

3.3/ CORNEAL LESIONS

The cornea is normally glossy, transparent and without visible blood vessels.

(§) Quantitative evaluations of the DEGREE AND EXTENT OF OPACITY of the cornea are scored according to the following system.

(§) To determine the presence or absence of corneal opacification and to evaluate the extent of surface attack a 2 % solution of fluorescein (CHIBRET) is instilled into the eye. Excess fluorescein is rinsed away with a jet of rinsing solution (DACYROSERUM - Chibret).

So that the results are not affected this method, which requires a rinse, is not conducted until after the reading made 1 hour after the instillation of the test substance.

Rinsing solution : when the details of the nature of the test substance are not known, the following solution is used as a rinsing agent : DACYROSERUM (CEJERET Laboratories - France)

- | | |
|-------------------------|-------|
| • Boric acid | 1,9 g |
| • Sodium borate | 1,2 g |
| • Sodium chloride | 0,3 g |

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- Degree of opacity (A)

(the most opaque area is chosen for the reading)

- . No opacity. Neither loss of brilliance nor gloss..... 0
- . Opacity scattered or diffuse, details of iris clearly visible..... 1
- . Translucent zone easily discernable, details of iris slightly obscured..... 2
- . Opalescent zone, no details of iris visible, size of pupil barely discernable..... 3
- . Cornea completely opaque, iris invisible..... 4

- Area of cornea affected (B)

- . One quarter (or less) but not zero..... 1
- . Greater than one quarter, up to one half 2
- . Greater than one half, up to three quarters 3
- . Greater than three quarters, up to whole area..... 4

Note : the total score is obtained by applying the formula :

A X B X 5 (maximum total : 80)

A qualitative evaluation of any ULCERATION or GRANULATION of the cornea is conducted to determine the irritative capacity of the test substance :

- Ulceration (loss of substance with or without swelling of the eye)

- . No ulceration..... 0
- . Presence of ulceration..... U

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- Area affected

- . One quarter (or less) but not zero a
- . Greater than one quarter, up to one half b
- . Greater than one half, up to three quarters c
- . From three quarters to total area d

Note : the best method for demonstrating the nature and degree of this lesion is the fluorescein test.

- Granulous dystrophy (multiple blisters spread over the corneal epithelium)

- . No granulation 0
- . Presence of granulation G

- Area affected

- . One quarter (or less) but not zero a
- . Greater than one quarter, up to one half b
- . Greater than one half, up to three quarters c
- . From three quarters to total area d

4/ INTERPRETATION OF RESULTS

The total number of eye lesions found in the conjunctiva, iris and cornea of each animal allows the calculation of the Individual Index of Ocular Irritation (I.I.O.I.) at each of the different observation times (1 hour and 1, 2, 3, 4 & 7 days after the instillation of the test substance).

A mean score per zone (conjunctiva, iris and corneal) is also calculated for the total of treated animals at 1 hour and 1, 2, 3, 4 & 7 days.

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The mean of the individual index of ocular irritation (I.I.O.I.) obtained at each observation time for the 6 rabbits treated allows the calculation of the "Mean Index of Ocular Irritation" (M.I.O.I.) and standard deviation and also to see the dispersion of the values within each group at different times.

The mean Indexes of Ocular Irritation (M.I.O.I.) obtained from readings at D 1, D 2 and D 3 are added and the sum is divided by 3.

This score enables the test substance to be classified, according to BASF specifications.

Classification of test substance

From 0 up to 10	NON IRRITANT
From 11 up to 25	SLIGHTLY IRRITANT
From 26 up to 56	MODERATELY IRRITANT
From 57 up to 110	STRONGLY IRRITANT

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R E S U L T S

OCULAR IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE : 77/930 : Corialverdünner EB

APPLICATION: 0.1 ml per animal of undiluted reference substance (without rinsing)DATE OF INSTILLATION : OCTOBER, 17th 1978

EVALUATION OF EFFECTS:		I H						D 1						D 2						
N° of rabbits :		313	314	315	316	317	318	313	314	315	316	317	318	313	314	315	316	317	318	
CONJUNCTIVA	A) Chaemosis	0 - 4	2	2	2	2	2	2	2	1	3	1	1	2	1	0	2	0	1	
	B) Discharge	0 - 3	2	1	1	2	1	2	2	1	0	2	0	0	1	0	0	2	0	0
	C) Enanthemea	0 - 3	2	2	1	2	2	2	2	0	2	1	1	2	1	0	2	0	1	
	(A + B + C) X 2 (max. = 20)	12	10	8	12	10	12	12	10	2	14	4	4	10	4	0	12	0	4	

DIRECT PHOTOMOTOR REFLEX OF PUPIL (\$)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
IRIS	Congestion	0 - 2	1	\$	1	\$	1	\$	1	1	\$	0	1	0	1	1	\$	1	\$	0	1	\$	0	0
	X 5 (max. = 10)	5	5	5	5	5	5	5	5	5	0	5	0	5	5	5	0	5	0	5	0	5	0	0

(\$: N = Normal

- R = Reduced

- No reflex

CORNEA	A) Opacity	0 - 4	1	1	1	2	1	1	1	1	1	0	2	1	1	0	0	0	0	0	0	0	0
	B) area affected)	1 - 4	1	1	1	1	1	1	1	1	1	0	1	1	1	0	0	0	0	0	0	0	0
	A X B X 5 (max. = 80)	5	5	5	10	5	5	5	5	0	10	5	5	0	0	0	0	0	0	0	0	0	0
	ULCERATION	0	U	0	0	0	0	0	U	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Area affected		a - d	/	a	/	/	/	a	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
GRANULATION		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Area affected		a - d	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Individual ocular irritation score IOI (max. : 110)	22	20	18	27	20	22	22	20	2	29	9	14	15	9	0	17	0	4

OBSERVATIONS: § Circumcorneal injection

° Circumcorneal injection + congestion of the iris.

MEAN SCORE PER ZONE	Conj. + Iris + Com.	Conj. + Iris + Com.	Conj. + Iris + Com.
	10.67	5.00	5.83

OCULAR IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE : 77/930 : Corialverdünner EB

APPLICATION : 0.1 ml per animal of undiluted reference substance (without rinsing)DATE OF INSTILLATION : OCTOBER, 17th 1978

EVALUATION OF EFFECTS :		D 3						D 4						D 7					
N° of rabbits :		313	314	315	316	317	318	313	314	315	316	317	318	313	314	315	316	317	318
CONJUNCTIVA	A) Chaemosis 0 - 4	2	1	0	2	0	0	1	1	0	2	0	0	0	0	0	1	0	0
	B) Discharge 0 - 3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	C) Enanthemea 0 - 3	1	1	0	2	0	0	1	1	0	2	0	0	0	1	0	1	0	0
	(A + B + C) X 2 (max. = 20)	6	4	0	8	0	0	4	4	0	8	0	0	0	2	0	4	0	0

DIRECT PHOTOMOTOR REFLEX OF PUPIL (\$)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
IRIS	Congestion 0 - 2	1	§	1	§	0	1	§	0	0	1	§	1	0	1	§	0	0	0
	X 5 (max. = 10)	5	5	0	5	0	0	5	5	0	5	0	0	0	5	0	0	0	0

(\$ N = Normal - R = Reduced - No reflex)

CORNEA	A) Opacity 0 - 4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	B) area affected) 1 - 4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	A X B X 5 (max. = 80)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	ULCERATION:	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Area affected a - d	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
	GRANULATION	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Area affected a - d	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Individual ocular irritation score IOI (max. : 110)	11	9	0	13	0	0	9	9	0	13	0	0	0	7	0	4	0	0
---	----	---	---	----	---	---	---	---	---	----	---	---	---	---	---	---	---	---

OBSERVATIONS :

§ Circumcorneal injection

MEAN SCORE PER ZONE	Conj. + Iris	+ Corn.	Conj. + Iris	+ Corn.	Conj. + Iris	+ Corn.
	3.00	2.50	0.00	2.67	2.50	0.00

6/ CONCLUSION:

The results found under the experimental conditions of this study are used to classify the test substance :

77/930 : Corialverdünner EB

following the scale mentioned above (B.A.S.F.)

	TIME ELAPSED AFTER INSTILLATION					
	1 hour	Day 1	Day 2	Day 3	Day 4	Day 7
TEST SUBSTANCE APPLIED UNDILUTED (WITHOUT RINSING)		21.5	16.0	7.5	5.5	5.2

The sum of Mean Indexes of Ocular Irritation (M.I.O.I.) obtained at 24, 48 and 72 hours = $16.0 + 7.5 + 5.5 = 29.0$

IRRITATION SCORE = $29.0 / 3 = 9.7$

NON-IRRITANT APPLICATION

DETERMINATION OF THE INDEX
OF PRIMARY CUTANEOUS IRRITATION
IN THE RABBIT

TEST FOR THE DETERMINATION OF THE INDEX
OF PRIMARY CUTANEOUS IRRITATION IN THE RABBIT

(following a method from "Code of Federal Regulations,
Title 16, Section 1500.42)

1/ OBJECTIVE

=====

This method is used to determine the primary irritation resulting from the application of a test substance. Primary irritants are those substances which, with a single application, cause an inflammatory cutaneous orthoergic reaction. The reaction is localised at the point of contact and appears within 24 hours of application.

The irritation depends upon the test substance, its concentration and the length of time it remains in contact with the skin.

2/ EXPERIMENTAL PROTOCOL

=====

2.1/ EXPERIMENTAL ANIMALS

Six male albino New Zealand white rabbits are used for each trial. They weigh between 2.5 kg and 3.5 kg at the start of the test, and they will have been vaccinated against pasteurellosis and myxomatosis. Only healthy animals without signs of skin lesions are selected for use.

2.2/ MAINTENANCE OF ANIMALS

The rabbits are kept in individual cages measuring 540 X 360 X 315 mm or in restraining devices which allow the back of the animal to be treated. The animal house is ventilated*. The ear of each animal is pierced and a metal tag (Chevillot : La Quick) attached for individual identification.

* Renewal of air = 12 times per hour

- Hygrometry = 55% ± 10 [Controlled with an Hygrometer-Thermometer :
- Temperature = 22°C Maudet Bourde - Jules Richard

200 g of food is provided per animal per day in the form of granules (Granulés Lapin "entretien" SANDERS). Water is given automatically and ad libitum.

2.3/ TEST METHOD

2.31/ PREPARATION OF THE SKIN

The six rabbits are clipped with a fine toothed electric clipper (AESCULAP - Type V 42 947) to bare a skin surface of 14 cm X 14 cm (The cutting height = 1/20e mm) ; thus a precise cut can be achieved without irritating the skin mechanically. The animals are left to rest for 24 hours and then only those with perfectly healthy skin are chosen for the test.

The right flank is scarified with a sterile scalpel blade, making three parallel superficial incisions 2 cm long and 0.5 cm apart. The incisions are epidermal and do not damage the dermis (should bleeding occur, a fresh animal is utilised).

2.32/ APPLICATION OF THE TEST SUBSTANCE

The compound¹ to be tested is applied to the rabbit skin, using the right, previously scarified flank and the left intact one, at a rate of 0.5 ml² per area and animal in the case of a viscous compound and at 0.5 g³ per area and animal when dealing with a powdery or pasty material (solid material -powder- is applied in paste form). These treated areas are subsequently covered with a 2 cm square gauze pad consisting of sterile, hydrophilic gauze of four layers. The material to be tested and the gauze pads are kept in contact with the skin by a patch⁴ (NEODERMOTEST ROC) consisting of a central, circular disc of 22 mm diameter with a surrounding adhesive, hypoallergenic, perforated plaster 10 mm wide.

¹ Product administered in its pure, undiluted form

² The volume of the product is measured and applied with a sterile, polypropylene syringe (Becton Dickinson) of 2.5 ml

³ Weighing done with a METTLER balance - type PL 200 ($d = 1 \text{ mg}$) and the material kept in a haemolysis tube.

⁴ Occlusive patches are used to keep the product in contact with the

Finally, an adhesive tape 6 cm wide is wound around the animal to complete the fixing of the patches. Care is taken so that the respiratory and abdominal movements of the animal are not restricted.

The rabbits are then placed for 24 hours in restraining devices.

2.4/ EVALUATION OF PRIMARY CUTANEOUS IRRITATION

After 24 hours of contact with the skin, the patches are removed. One hour later, the primary irritation index is evaluated and the animals are then put back into their individual cages. 48 hours later, a second reading is made to determine the extent of any recovery (the two readings are performed respectively 25 and 72 hours after the application of the substance).

If after the last reading, any irritation is noted, the animals are maintained under observation for one week. On the 7th day, another reading is made, special attention to be paid to the presence of desquamation at the site of application.

Readings are made of both the scarified and non scarified zones, following the scale of scores proposed by the "Journal Officiel", as shown below.

Erythematous (and scar) lesions

- No erythema..... 0
- Very slight erythema (barely perceptible)..... 1
- Well defined erythema..... 2
- Moderate to severe erythema..... 3
- Severe erythema, crimson red, with slight eschar formation (injuries in depth)..... 4

Oedematous lesions

- No oedema..... 0
- Very slight oedema (barely perceptible)..... 1
- Slight oedema (edges of area well defined by definite raising)..... 2
- Moderate oedema (area raised approximately 1 mm)..... 3
- Severe oedema (raised more than 1 mm and

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2.5/ SCORING

The scores obtained on the normal and abraded zones of each animal, for erythema and oedema respectively, are added at 25 and 72 hours.

Each of the 8 total scores are divided by 6 (number of rabbits per test) or by the number of animals for which a reading was possible.

A mean value at a given time (25 and 72 hours) is thus obtained for each reading. These means are added for erythema (ΣE) and for oedema (ΣO).

The sum of the erythema means (ΣE) and that of the oedema (ΣO) is divided by 4 ($\frac{\Sigma E + \Sigma O}{4}$) ; the figure obtained (never above 8) represents the Primary Cutaneous Irritation Index.

This index allows to classify the test substance as follows :

<u>Index of primary irritation</u>	<u>Classification of the test material</u>
From 0.0 up to 0.5	NON-IRRITANT
From 0.6 up to 3.0	SLIGHTLY IRRITANT
From 3.1 up to 5.0	MODERATELY IRRITANT
From 5.1 up to 8.0	SEVERELY IRRITANT

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- 3 -

R E S U L T S

PRIMARY CUTANEOUS IRRITATION TEST IN THE RABBIT - RESULTS

TEST SUBSTANCE: 77/930 : Corialverdünner EB

APPLICATION: 0.5 ml per zone, per animal of undiluted reference substance.DATE OF APPLICATION: OCTOBER, 18th 1978

RABBITS N°		433	434	435	436	437	438bis	TOTAL	MEAN
ERYTHEMA	NORMAL	25 h.	0	0	0	0	0	0	0.0
	SCARIFIED	72 h.	0	0	0	0	0	0	0.0
		7 d.	0	0	S	0	0	S	
SCARIFIED	25 h.	0	1	1	0	1	0	3	0.5
	72 h.	0	1	0	0	1	0	2	0.3
	7 d.	0	S	S	0	S	S		ΣE
									0.8

RABBITS N°		433	434	435	436	437	438bis	TOTAL	MEAN
OEDEMA	NORMAL	25 h.	0	0	0	0	0	0	0.0
	SCARIFIED	72 h.	0	0	0	0	0	0	0.0
		7 d.	0	0	0	0	0	0	
SCARIFIED	25 h.	0	0	0	0	0	0	0	0.0
	72 h.	0	0	0	0	0	0	0	0.0
	7 d.	0	0	0	0	0	0		ΣO
									0.0

OBSERVATIONS: S = Slight desquamation

Rabbit n° 438 died on October, 19th 1978, and was replaced by another animal numbered 438 bis.PRIMARY CUTANEOUS IRRITATION SCORE $(\frac{\Sigma E + \Sigma O}{4})$

SAMPLE CLASSIFICATION

Non-irritant: 0.0 - 0.5
Slightly Irritant: 0.6 - 1.0

Substanz: Corialmattierung G

Substanz-Nr.: XXVI 561

ERGEBNIS DER GEWERBETOXIKOLOGISCHEN GRUNDPRÜFUNG

1. AKUTE ORALE TOXIZITÄT (Ratte):
 $LD_{50} > 10000 \text{ mg/kg.}$

2. AKUTES INHALATIONSRISIKO (3):

Akutes Inhalationsrisiko (Ratte; abhängig von Toxizität UND Flüchtigkeit; Rückschlüsse auf die akute Inhalationstoxizität sind nicht möglich):

Nach 8 Stunden Exposition in einer bei 20 °C angereicherten Atmosphäre keine Tiere gestorben.

3. PRIMÄRE HAUTREIZWIRKUNG (geprüft am Kaninchen nach (6)):

Primärer Reizwert: 0,54 (vgl. 6)

Aufgrund der Befunde muß die Substanz als NICHT REIZEND bezeichnet werden.

4. PRIMÄRE SCHLEIMHAUTREIZWIRKUNG (geprüft am Kaninchenauge nach (6)):

Primärer Reizwert: 29 (vgl. 6)

Aufgrund der Befunde muß die Substanz als MÄSSIG bis STARK REIZEND bezeichnet werden.

Bei Einwirkung der Substanz auf die Augen muß mit HORNHAUTTRÜBUNGEN gerechnet werden.

Die pathologischen Befunde am Auge und die Reizerscheinungen an der Schleimhaut bildeten sich innerhalb von 7 Tagen nicht zurück.

S I C H E R H E I T S R A T S C H L Ä G E :

VORSICHT! Augen SORGFÄLTIG schützen.

Im Übrigen sind die beim Umgang mit Chemikalien allgemein üblichen Vorsichtsmaßregeln zu beachten.

B E S O N D E R E B E M E R K U N G E N :

AKUTE INTRAPERITONEALE TOXIZITÄT (Maus): 720 mg/kg.

Isopropanol, Xylol, Butylacetat sind in der Arbeitsstoff-Verordnung (Anhang I), MAK-Liste und EG-Liste zur Kennzeichnung gefährlicher Stoffe aufgeführt. Die nicht berücksichtigten Konsequenzen sind zu

Substanz: Corialmattierung G

Substanz-Nr.: XXVI 561

- a) Vorschlag für die ZUORDNUNG VON R- UND S-SÄTZEN (Amtsblatt der EG, 30.12.76, 76/907/EWG):

R: 36 = Reizt die Augen

S: 25 = Berührung mit den Augen vermeiden

- b) Vorschlag zum Gefahrensymbol: Xi = reizend

Die Zuordnung der R- und S-Sätze sowie des Gefahrensymbols stützt sich allein auf die Haut- und Schleimhautreizwirkung und die orale Toxizität.

(3) In Anlehnung an H.F. Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107 (1962)

(6) Federal Register 38 No 187 § 1500.41 (Haut) und § 1500.42 (Auge), S. 27019 vom 27.09.73.

Bewertung nach: Draize, J.H. (1959): Dermal Toxicity. In: FDA-Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics.


Dr. med. Hofmann


Dr. med. habil. Dr. rer. nat. Gelbke

BASF Aktiengesellschaft

BASF

Safety data sheet
according to 91/155/EEC

Page 1 of 4

BASF Safety data sheet
Date / revised: 25.08.1993
Product: LUMITOL® M 81

ED 01015-3 /F/D
version 1

1. Trade name:

LUMITOL® M 81

Company:
BASF Aktiengesellschaft
Marketing Dispersionen
D-67056 Ludwigshafen
Tel.: 0621-60-0

Emergency information:
Firebrigade Ludwigshafen
Tel.: 0621-60-43333

Fax: 0621-60-92664

2. Composition/information on ingredients

Chemical nature
acrylic resin, containing hydroxyl groups, approx. 65% solution in:
1-methoxy-2-propylacetate

3. Possible hazards

Critical hazards to man and the environment:
R10 - Flammable.

4. First aid measures

General advice: immediately remove contaminated clothing.

If danger of loss of consciousness, place patient in recovery position and transport accordingly. Apply artificial respiration if necessary.

If inhaled: keep patient calm, remove to fresh air, summon medical help

On skin contact: wash with soap and water.

On contact with eyes: wash affected eyes for at least 15 minutes under running water with eyelids held open, consult an eye specialist.

On ingestion: keep patient calm, remove to fresh air, summon medical help

5. Fire fighting measures

Suitable extinguishing media:
water spray, foam, carbon dioxide (CO₂), dry extinguishing media

6. Accidental release measures

methods for cleaning up

Contain with absorbent material (e.g. sand, silica gel, acid binder, general purpose binder, sawdust).

7. Handling and storage

Handling

Protection against fire and explosion:
Source of ignition should be kept clear. Take precautionary measures
against static discharges.



8. Exposure controls and personal protection

Additional information on the lay-out of technical plant
 (see 7)

Components with workplace control parameters

The values and other data of TRGS 900 (Germany) must be observed.

1-methoxy-2-propylacetate, 108-65-6
 styrene, 100-42-5
 ethylbenzene, 100-41-4

Personal protective equipment

Hand protection: solvent-resistant gloves

Eye protection: goggles

General safety and hygiene measures:

Keep away from foodstuffs, animal feedstuffs and beverages. Hands and/or face should be washed before breaks and at the end of the shift.

9. Physical and chemical properties

Form: liquid

Colour: colourless - faint yellow

Odour: of solvent

Change in physical state

Melting point/melting range: °C

Boiling point/boiling range: 145 - 151 °C

Flash point: 48 °C DIN 53 213

Combustibility:

Explosion limits:

- lower	1.5 Vol.% 1-Methoxyprop.ac.-2
- upper	10.8 Vol.% (20 °C, 1013 mbar)

Ignition temperature: 315 °C DIN 51 794

Vapour pressure: (20 °C) 3 mbar
 (50 °C) 21 mbar

Density: (20 °C) 1.0 g/cm³

Solubility in water: (20 °C) 200 g/l
 1-Methoxypropac.-2

pH value: not applicable

Viscosity: (23 °C) 1300-1800 mPa.s DIN 53 019

10. Stability and reactivity

Thermal decomposition:
 No decomposition if used correctly.

Hazardous reactions:
 No decomposition if used correctly.

BASF Safety data sheet
 Date / revised: 25.08.1993
 Product: LUMITOL® M 81

ED 01015-3 /F/D
 version 1

11. Toxicological information

Acute toxicity

The statement was derived from products of similar composition.

LD50/oral/rat: > 10 000 mg/kg

Primary skin irritation/rabbit/: non-irritant

Primary mucous membrane irritation/rabbits' eyes/: non-irritant

12. Ecological information

elimination information

Do not discharge product into natural waters without pretreatment (biological treatment plant).

The solvent is biodegradable.

Solubility in water: partly soluble.

Behaviour and environmental fate

Inhibition of degradation activity in activated sludge not to be anticipated during correct introduction of low concentrations.

The insoluble fraction can be removed by mechanical means in suitable waste water treatment plants..

Ecotoxic effects

No data available.

Further ecological information

Local effluent treatment regulations should be complied with.

13. Disposal considerations

Must be disposed of by special means, e.g. suitable incineration, in accordance with local regulations.

14. Transport information

Land transport

ADR/RID/GGVS/GGVE	Class: none	Item number/letter:
Warning panel	Hazard-no:	Substance no.:
UN-No:		
Description of the goods:		
Remarks:		

Inland waterway transport

ADN/ADNR	Class: none	Item number/letter:
		Category:
Description of the goods:		
Remarks:		

Sea transport

IMDG/GGVSee	Class: 3.3	UN-No: 1866 PG: III
	EMS: 3-05	MFAG: 310
Marine pollutant: no		
Proper technical name: Resin solution in flammable liquid (contains Methoxypropylacetate).		
Remarks:		

Air transport

ICAO/IATA	Class: 3	UN/ID-No.: 1866 PG: III
Proper technical name: Resin solution in flammable liquid (contains		

15. Regulatory information

Labelling according to EEC Directives

R10 - Flammable.

S24/25 - Avoid contact with skin and eyes.

The usual precautions for the handling of chemicals must be observed.

National legislation/regulations

Water hazard class: WGK (1) (Germany) (BASF self-classification)

16. Other information

A backslash in the left hand margin indicates an amendment from the previous version.

The information contained herein is based on the present state of our knowledge and does not therefore guarantee certain properties.
Recipients of our product must take responsibility for observing existing laws and regulations.

BASF Aktiengesellschaft

Safety data sheet
according to 91/155/EEC

BASF

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BASF Safety data sheet
Date / revised: 13.09.1993
Product: BASONAT® P LR 8772

ED 00895-3

/F/D

version 2

1. Trade name:

BASONAT® P LR 8772

Company:

BASF Aktiengesellschaft
Marketing Dispersionen
D-67056 Ludwigshafen
Tel.: 0621-60-0

Emergency information:

Firebrigade Ludwigshafen
Tel.: 0621-60-43333

Fax: 0621-60-92664

2. Composition/information on ingredients

Chemical nature

polyfunctional isocyanate, aromatic, approx. 67% solution in
1-methoxy-2-propylacetate / xylene in ratio 1:1

hazardous ingredients

CAS-No. 1330-20-7 xylene
Content: 16,5 % weight
R-phrases: 10-20/21-38

Hazard symbol: Xn

3. Possible hazards

Critical hazards to man and the environment:
R20 - Harmful by inhalation.

4. First aid measures

General advice: immediately remove contaminated clothing.

If danger of loss of consciousness, place patient in recovery position and transport accordingly. Apply artificial respiration if necessary.

If inhaled: keep patient calm, remove to fresh air, administer dexamethasone aerosol without delay.

On skin contact: wash thoroughly with soap and water.

On contact with eyes: wash affected eyes for at least 15 minutes under running water with eyelids held open, consult an eye specialist.

5. Fire fighting measures

Suitable extinguishing media:

water spray, carbon dioxide (CO₂), foam, dry extinguishing media

6. Accidental release measures

Methods for cleaning up:

Sweep/shovel up; soak up remainder with absorbent material (e.g. sand, Kieselgur).

7. Handling and storage

Handling

Protection against fire and explosion:

In case of fire, wear a self contained breathing apparatus.

Storage

If moisture enters isocyanate containers CO₂ forms and the pressure builds up.

Do not store together with: amines or products containing amines, substances that contain groups with active hydrogen.

Ensure thorough ventilation of stores and work areas.

8. Exposure controls and personal protection

Additional information on the lay-out of technical plant
 (see 7)

Components with workplace control parameters

The values and other data of TRGS 900 (Germany) must be observed.

toluene-2,6-diisocyanate, 91-08-7
 xylene, 1330-20-7

Personal protective equipment

Hand protection: protective gloves

Eye protection: goggles

General safety and hygiene measures:

Keep away from foodstuffs, animal feedstuffs and beverages. Avoid contact with the skin, eyes and clothing. Hands and/or face should be washed before breaks and at the end of the shift.

9. Physical and chemical properties

Form: liquid

Colour: colourless to faint yellowish

Odour: of solvent

Boiling point/boiling range: 145 °C

Flash point: 38 °C DIN 53 213

Explosion limits:

- lower 1.0 Vol.% 1-Meth.prop.ac.-2/ Xylol
 - upper 10.8 Vol.% (20 °C, 1013 mbar)

Ignition temperature: 500 °C DIN 51 794

Vapour pressure: (20 °C) 11 mbar
 (50 °C) 47 mbar

Density: (20 °C) 1.15 g/cm³

Solubility in water: (°C) not applicable

pH value: (at g/l, °C) not applicable

Viscosity: (23 °C) 1300-2300 mPa.s DIN 53 019

10. Stability and reactivity

Thermal decomposition:
 No decomposition if used correctly.

11 12 13 14

Hazardous reactions:

if moisture enters isocyanate containers CO₂ forms and the pressure builds up.

Hazardous reaction influenced by: alcohols, amines or products containing amines, water, substances that contain groups with active hydrogen.

11. Toxicological information

Acute toxicity

LD₅₀/oral/rat: > 5 000 mg/kg

LC₅₀/inhal./rat: > 3,8 mg/l / 4 h als Aerosol

primary mucous membrane irritation/rabbits' eyes/BASF test: irritant

primary skin irritation/rabbit/BASF test: slight irritant

12. Ecological information

Elimination information

Do not discharge product into natural waters without pretreatment (biological treatment plant).

Reacts slowly with water at the interface and liberates CO₂ to form an insoluble polyurea with a high melting point.

Can be separated from water mechanically in effluent treatment plants.

The solvent is biodegradable.

Behaviour and environmental fate

Insoluble polymerized urea can clog pipelines and cleaning equipment.

Ecotoxic effects

No data available.

Further ecological information

Local effluent treatment regulations should be complied with.

13. Disposal considerations

Must be disposed of by special means, e.g. suitable incineration, in accordance with local regulations.

14. Transport information

Land transport

ADR/RID/GGVS/GGVE

Class: none

Item number/letter:

Warning panel

Hazard-no:

Substance no.:

UN-No:

Description of the goods:

Remarks:

Inland waterway transport

ADN/ADNR

Class: none

Item number/letter:

Category:

Description of the goods:

BASF Safety data sheet
Date / revised: 13.09.1993
Product: BASONAT® P LR 8772

ED 00895-3 /F/D
version 2

Sea transport
IMDG/GGVSee

Class: 3.3
EMS: 3-05

UN-No: 1866 PG: III
MFAG: 310

Marine pollutant: no
Proper technical name: Resin solution in flammable liquid (contains Xylol and Methoxypropylacetate).

Remarks:

Air transport

ICAO/IATA Class: 3 UN/ID-No.: 1866 PG: III
Proper technical name: Resin solution in flammable liquid (contains Xylol and Methoxypropylacetate).

Remarks:

15. Regulatory information

Labelling according to EEC Directives

Contains: polyfunctional isocyanate and xylene

Xn - Harmful

R10 - Flammable.

R20/21 - Harmful by inhalation and in contact with skin.

R36 - Irritating to eyes.

S37 - Wear suitable gloves.

Handle in accordance with good industrial hygiene and safety practice.

National legislation/regulations

Water hazard class: WGK (2) (Germany) (BASF self-classification)

16. Other information

A backslash in the left hand margin indicates an amendment from the previous version.

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Recipients of our product must take responsibility for observing existing laws and regulations.

BASF Aktiengesellschaft

Safety data sheet
according to 91/155/EEC

BASF

Page 1 of 4

BASF Safety data sheet
Date / revised: 02.12.1993
Product: BASONAT® HB 175 MP/X

ED 00694-3 /F/D
version 4

(Print date: 04.02.1994)

1. Substance/preparation and company name

BASONAT® HB 175 MP/X

Company:

BASF Aktiengesellschaft
Marketing Dispersionen
D-67056 Ludwigshafen
Tel.: 0621-60-0

Emergency information:

Firebrigade Ludwigshafen
Tel.: 0621-60-43333

Fax: 0621-60-92664

2. Composition/information on ingredients

Chemical nature

Polyfunctional isocyanate, aliphatic, approx. 75% solution in
Methoxypropyl acetate / xylene in ratio 1:1.

Hazardous ingredients

CAS-No. 1330-20-7 xylene
Content: < 12,5 % weight
R-phrases: 10-20/21-38

Hazard symbol: Xn

3. Possible hazards

Critical hazards to man and the environment: flammable.

4. First aid measures

General advice: Immediately remove contaminated clothing.

If danger of loss of consciousness, place patient in recovery position and transport accordingly. Apply artificial respiration if necessary.

If inhaled: Keep patient calm, remove to fresh air, administer dexamethasone aerosol without delay.

On skin contact: Wash thoroughly with soap and water.

On contact with eyes: Wash affected eyes for at least 15 minutes under running water with eyelids held open, consult an eye specialist.

5. Fire fighting measures

Suitable extinguishing media:
water spray, carbon dioxide (CO₂), foam, dry extinguishing media

6. Accidental release measures

Methods for cleaning up:

Sweep/shovel up; soak up remainder with absorbent material (e.g.

7. Handling and storage

Handling

Protection against fire and explosion:

In case of fire, wear a self contained breathing apparatus.

Take precautionary measures against static discharges.

Storage

If moisture enters isocyanate containers CO₂ forms and the pressure builds up.

Do not store together with: amines or products containing amines, substances that contain groups with active hydrogen.

Ensure thorough ventilation of stores and work areas.

8. Exposure controls and personal protection

Additional information on the lay-out of technical plant
(see 7)

Components with workplace control parameters

The values and other data of TRGS 900 (Germany) must be observed.

1,6-hexamethylene diisocyanate, CAS-No. 822-06-0
xylene, CAS-No. 1330-20-7

Personal protective equipment

Hand protection: protective gloves

Eye protection: goggles

General safety and hygiene measures:

Keep away from foodstuffs, animal feedstuffs and beverages. Avoid contact with the skin, eyes and clothing. Hands and/or face should be washed before breaks and at the end of the shift.

9. Physical and chemical properties

Form: liquid

Colour: colourless to faint yellowish

Odour: of solvent

Boiling point/boiling range: > 120 °C

Flash point: 39 °C DIN 55 679

Explosion limits:

- lower 1.0 Vol.%
- upper 10.8 Vol.%

Ignition temperature: . 460 °C DIN 51 794

Vapour pressure: (20 °C) 10 mbar

Density: (20 °C) 1.07 g/cm³

Solubility in water: (20 °C) 200 g/l 1-Methoxypropylac.-2

pH value: (at g/l, °C) not applicable

Viscosity: (20 °C) 130 - 300 mPa.s DIN 53 519

BASF Safety data sheet
Date / revised: 02.12.1993
Product: BASONAT® HB 175 MP/X

ED 00694-3 /F/D
version 4

10. Stability and reactivity

Thermal decomposition:
No decomposition if used correctly.

Hazardous reactions:
If moisture enters isocyanate containers CO₂ forms and the pressure builds up.

Hazardous reaction influenced by: alcohols, amines or products containing amines, water, substances that contain groups with active hydrogen.

11. Toxicological information

Acute toxicity
The statement was derived from products of similar composition.

LD₅₀/oral/rat: > 5000 mg/kg

Primary skin irritation/rabbit/OECD-Test: non-irritant

12. Ecological information

Elimination information

Do not discharge product into natural waters without pretreatment (biological treatment plant).

The product is difficultly soluble in water.

Can be separated from water mechanically in effluent treatment plants.

The solvents are biodegradable.

Behaviour and environmental fate

Reacts slowly with water at the interface and liberates CO₂ to form an insoluble polyurea with a high melting point.

Ecotoxic effects no data available

Further ecological information

Local effluent treatment regulations should be complied with.

13. Disposal considerations

Must be disposed of by special means, e.g. suitable incineration, in accordance with local regulations.

14. Transport information

Land transport

ADR/RID/GGVS/GGVE Class: 3 Item number/letter: 31 c)
Warning panel Hazard-no: 30 Substance no.: 1866

UN-No: -

Description of the goods:

Remarks:

Inland waterway transport

ADN/ADNR Class: 3 Item number/letter: 3
Category: K2

Description of the goods:

1 2 3 4 5

BASF Safety data sheet
Date / revised: 02.12.1993
Product: BASONAT® HB 175 MP/X

ED 00694-3 /F/D
version 4

Sea transport

IMDG/GGVSee

Class: 3.3

UN-No: 1866 PG: III

EMS: 3-05

MFAG: 310

Marine pollutant: no

Proper technical name: Resin solution in flammable liquid (contains Xylol).

Remarks:

Air transport

ICAO/IATA

Class: 3

UN/ID-No.: 1866 PG: III

Proper technical name: Resin solution in flammable liquid (contains Xylol).

Remarks:

15. Regulatory information

Labelling according to EEC Directives

Contains: polyfunctional isocyanate

R10 - Flammable.

S23 - Do not breathe vapour and spray

S24/25 - Avoid contact with skin and eyes.

Handle in accordance with good industrial hygiene and safety practice.

National legislation/regulations

Water hazard class: WGK (2) (Germany) (BASF self-classification)

16. Other information

A backslash in the left hand margin indicates an amendment from the previous version.

The information contained herein is based on the present state of our knowledge and does not therefore guarantee certain properties.
Recipients of our product must take responsibility for observing existing laws and regulations.

Substanz:

- 3 -

Vers.Nr.

Corial-Finish EC

XXIV 186

bzw. LD 50

TOXIZITÄT akut: approximative - mittlere letale Dosis = A LD 50 berechnet nach LITCHFIELD-WILCOXON

Applikationsform:

15-35%ige Emulsion in 0,5%iger wässriger Carboxymethylcellulose-Zubereitung

A LD 50 je kg Körpergewicht, Beobachtungszeit 7/14 Tage

Maus i.p. ca. 2000 µl

Ratte p.o. 7200 (6545-7920)µl

Symptome:

Mäuse: krampfartiges Zucken, Apathie, Taumeln, Atonie, Dyspnöe, Bauch-Seiten- und Rückenlage.

Ratten: krampfartiges Zucken, Zittern, Taumeln, Apathie, Atonie, Dyspnöe, Speichelfluß.

Sektion: Mäuse: teilweise intraabdominelle Niederschläge und Verklebungen.

Ratten: akute Herzdilatation und Stauungshyperämie, lehmfarbener Beiton der Leber.

Munk
gez. Dr. Munk

Fleisberg
gez. Dr. Fleisberg

AKUTE INHALATIONSTOXIZITÄT (Ratte = R; Meerschweinchen = Me; Maus = Ma)

Inhalation einer mit Dampf bei 20°C gesättigten Atmosphäre. Zur Sättigung XXIX Minuten benötigt.

Meerschweinchen wurde durch eine ca. 5 cm hohe Schicht des Produktes Luft geleitet (starke/schwache Staubentwicklung)

Expositionzeit:

3' 10' 30' 1^h 3^h 8^h

a) Dampf bei 20°C (R)

0/12 Mortalität x/y
gestorbene/exponierte Tiere

b) Dampf bei 0°C

c) Staub

d) Spray sig
in

Symptome: Gleichgewichtsstörungen.

Hofmann
gez. Dr. Hofmann

Sektion: o.B.

Fleisberg
gez. Dr. Fleisberg

HAUTREIZ (Kaninchen)

Einwirkungszeit

Befund nach 24 Std.

Befund nach 8 Tagen

Applikationsform:

Rücken 1'

unverdünnt

5'

15'

Rücken 20'

Ø

Ø

R (+)

Ohr 20^h

R +

klebrige Substanzreste

Ø

SCHLEIMHAUTREIZ (Kaninchenauge)

Befund nach 1 Std.

Befund nach 24 Std.

Befund nach 8 Tagen

Applikationsform:

(1 x 50 mm² bzw. 50 mg)
unverdünnt

R+/Ö++/Tr++

R++/Ö+/Tr++

Ø

schmierige Auflage

Vergleich: NaCl

Ø

Ø

Ø

Zeichenerklärung für Haut- und Schleimhautreiz:

Munk

Substanz: Corialfinish EC

Substanz-Nr.: 77/856

ERGEBNIS DER GEWERBETOXIKOLOGISCHEN GRUNDPRÜFUNG

1. AKUTE ORALE TOXIZITÄT (Ratte):
LD₅₀ > 5 000 mg/kg.

2. AKUTES INHALATIONSRISIKO (3):

Akutes Inhalationsrisiko (Ratte; abhängig von Toxizität UND Flüchtigkeit; Rückschlüsse auf die akute Inhalationstoxizität sind nicht möglich):

Nach 7 Stunden Exposition in einer bei 20°C angereicherten Atmosphäre keine Tiere gestorben. Im Versuch wurden Reizerscheinungen an Augen und Atemorganen beobachtet.

3. PRIMÄRE HAUTREIZWIRKUNG (geprüft am Kaninchen nach (5) und (6)):

Primärer Reizwert: 3,3 (vgl. 6)

Aufgrund der Befunde muß die Substanz als MÄSSIG REIZEND bezeichnet werden.

Die Veränderungen traten schon nach kurzer Einwirkungsdauer auf. Die Reizerscheinungen bildeten sich innerhalb von 8 Tagen zurück.

4. PRIMÄRE SCHLEIMHAUTREIZWIRKUNG (geprüft am Kaninchenauge nach (6)):

Primärer Reizwert: 28 (vgl. 6)

Aufgrund der Befunde muß die Substanz als MÄSSIG REIZEND bezeichnet werden.

Bei Einwirkung der Substanz auf die Augen muß mit HORNHAUTTRÜBUNGEN und ENTZÜNDUNGEN AN DER REGENBOGENHAUT gerechnet werden.

Die pathologischen Befunde am Auge und die Reizerscheinungen an der Schleimhaut bildeten sich innerhalb von 8 Tagen zurück.

Substanz: Corialfinish EC

Substanz-Nr.: 77/856

S I C H E R H E I T S R A T S C H L Ä G E :

Länger dauerndes Einatmen vermeiden.
Augen vor Dämpfen und flüchtigen Anteilen schützen.
Berührung mit der Haut SORGFÄLTIG vermeiden.
Augen SORGFÄLTIG schützen.

Im übrigen sind die beim Umgang mit Chemikalien allgemein üblichen Vorsichtsmaßregeln zu beachten.

B E S O N D E R E B E M E R K U N G E N :

a) Vorschlag für die ZUORDNUNG VON R- UND S-SÄTZEN (Amtsblatt der EG, 30.12.76, 76/907/EWG):

R: 36/37/38 = Reizt die Augen, Atmungsorgane und die Haut
S: 24/25 = Berührung mit den Augen und der Haut vermeiden
S: 23 = Gas/Rauch/Dampf/Aerosol nicht einatmen

b) Vorschlag zum Gefahrensymbol: Xi = reizend

Äthylglykolacetat, n-Butylacetat und Butanol sind im Anhang I der Arbeitsstoff-Verordnung und in der MAK-Liste aufgeführt. Die sich daraus ergebenden Konsequenzen sind zu beachten.

Die Zuordnung der R- und S-Sätze sowie des Gefahrensymbols stützt sich allein auf die Haut- und Schleimhautreizwirkung und die orale und mit Einschränkung die inhalatorische Toxizität.

(3) In Anlehnung an H.F. Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107 (1962)

(5) BASF-Methode

(6) Federal Register 38 No 187 § 1500.41 (Haut) und § 1500.42 (Auge), S. 27019 vom 27.09.73.
Bewertung nach: Draize, J.H. (1959): Dermal Toxicity. In: FDA-Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics.


Dr. med. Hofmann


Dr. med. habil. Dr. rer. nat. Gelke

77 / 856 RATTE / ORAL

BLATT 1

AKUTE TOXIZITAET
=====

SUBSTANZ NUMMER I 77 / 856
I
SUBSTANZ NAME I CORIALFINISH EC
I
LOESUNGSMITTEL I 0.5% WAESS. CARBOXYMETHYLCELLULOSE ZUBER.
I
APPLIKATIONSFORM I EMULSION
I
APPLIKATIONSAART I ORAL
I
TIERART I RATTE/SPRAGUE DAWLEY/WIGA
I
FUTTER I HERKLAER HKH-HALTUNG; H. EGGERSMANN KG
I
NUECHTERNPERIODE I 15H - 20H VOR APPL.
I
BEZOEGHTUNGSDAUER I 14 D
I
DATUM DER APPL. I 13. 4. 78
I

DOSIS MG/KG I 5000.00 I
I I
KONZ. % (G/V) I 50.00 I
I I
APPL.VOL. ML/KG I 10.00 I
I I

ERGEBNIS

LD50 NACH 14 D

M+W : GROESSER: 5000.00 (MG/KG) (1 % SIGNIFIKANZLEVEL)

VERSUCHSDURCHFUEHRUNG : (DR. HERR. HABIL. DR. RER. NAT. (GELEHR.) 

SYMBOLE : D = "TAG" ; H = "STUNDE"
M = MAENNLICH ; W = WEIBLICH

77 / 856 RATTE / ORAL

BLATT 2

AKUTE TOXIZITAET
=====

SYMPTOME :

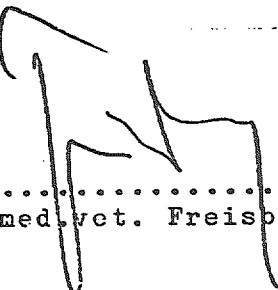
DOSIS MG/KG | 5000.00 |
 | |

KEINE AUFFAELLIGKEITEN

SEKTIONSBEFUNDE:

Getötete Tiere:

Organe o.B.



.....
Dr.med.vct. Freisberg

AKUTE TOXIZITÄT
=====

DOSIS MG/KG I 5000.00 I
 I I

MORTALITÄT:

	M	I	
TIERE ZU BEGINN	I	5	I
	I		
TOTE TIERE NACH	I		
1 H I	0	I	
1 D I	0	I	
2 D I	0	I	
7 D I	0	I	
14 D I	0	I	

	W	I	
TIERE ZU BEGINN	I	5	I
	I		
TOTE TIERE NACH	I		
1 H I	0	I	
1 D I	0	I	
2 D I	0	I	
7 D I	0	I	
14 D I	0	I	

MITTELGEW. (G):

	M	I	
ZU BEGINN	I	230.00	I
	I		
NACH:	I		
2-4D I	262.00	I	
7 D I	287.00	I	
10 D I	305.00	I	

	M	I	
ZU BEGINN	I	180.00	I
	I		
NACH:	I		
2-4D I	198.00	I	
7 D I	206.00	I	
10 D I	210.00	I	

77 / 856 RATTE / ORAL

BLATT 4

AKUTE TOXIZITAET
=====

LD50-BESTIMMUNG : BEOBUCHTUNGSDAUER 14 D
----- TIERE MAENNLICH UND WEIBLICH

DOSEN (MG/KG)	ANZAHL TIERE	TOTE TIERE NACH 14 D	MORTA- LITAET (%)	DOSEN VER- WENDET
5000.00	10	0	0%	*

LD50-WERT > 5000.00 (1 % SIGNIFIKANZLEVEL)

28.8.78

400d

Substanz: Corialfinish EC

Substanz-Nr.: 77/856

5

AKUTE HAUTREIZWIRKUNG

Applikationsform: unverändert

Einwirkungszeit	TierNr.	1. Rötung - Veräzung			2. Ödem		
		24 Std	48 Std	8 Tage	24 Std	48 Std	8 Tage
RÜCKEN	5 min	1	2 ü	2 ü	0 S	2	0
		2	2	2 ü	0	0	0
	2 Std	1	2 ü	2 ü	1 S	2	0
		2	2 ü	2 ü	1 S	0	0

ZETCHENERKLÄRUNG/HAUTREIZWIRKUNG:

Rötung: 1 = fraglich, 2 = leicht, 3 = stark, 4 = sehr stark;
Ödem: 1 = sehr leicht, 2 = leicht, 3 = stark, 4 = sehr stark;
S = Schuppenbildung; sS = starke Schuppenbildung
N = Nekrose (w = weich, p = pergamentartig, l = lederartig,
h = hart verschieblich, t = tiefgreifend, fl = fleckig nekrotisch)
Na = Narben; ü = übergreifend; id = induriert

.....
Dr.med.habil.Dr.rer.nat. Gelbke



az: Corialfinish EC

Substanz-Nr.: 77/856

HAUTREIZWIRKUNG (Einzelwerte) am Kaninchen; Methoden gemäß Federal Register 28, No. 197, § 1500.41, S. 27029 vom 27.09.73

ationsform: unverändert

Zeit	Hautreizwirkung/Tier Nr.						Σ	%
	1	2	3	4	5	6		
autrötung ntakt	24 h	1	2	2	2	2	11	1,8
	72 h	2	2	2	2	2	12	2,0
	8 d	0 S	0 S	0 S	1 S	0 S	0 S	
kerifi- ziert	24 h	2	3	3	2	2	3	2,5
	72 h	2 ü	2	2	2	2	2	2,0
	8 d	0 S	0 S	0 S	1 S	1 S	1 S	
dembildung ntakt	24 h	0	1	0	0	2	2	0,8
	72 h	1	0	0	0	0	2	0,5
	8 d	0	0	0	0	0	0	
karifi- ziert	24 h	0	2	2	2	2	3	1,8
	72 h	2 ü	1	2	1	2	10	1,7
	8 d	0	0	0	0	0	0	

Der Reizwert: $\frac{13,1}{4} = 3,3$

Bemerkungen: mäßig reizend

13,1

ERKLÄRUNG siehe letzte Seite

Müller
Dr.habil.rer.nat. Gelbke

LEIMHAUTREIZWIRKUNG (Einzelwerte); Methoden gemäß Federal Register 28, No. 187, § 1500.41, S. 27019 vom 27.09.73

onsform: unverändert

en	24 Stunden						48 Stunden						72 Stunden						nach 8 Tagen					
	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
26	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	0	0	0	0
16	4	4	4	4	0	4	4	4	4	0	4	4	4	3	4	3	4	4	0	4	0	0	0	0
)	20	20	20	20	0	20	20	20	20	0	20	20	20	15	20	20	20	20	0	0	0	0	0	0
)	Pv	1	1	0	0	Pv	1	1	1	1	0	Pv	1	0	Pv	1	0	Pv	1	0	0	0	0	0
)	5	5	5	5	0	0	5	5	5	5	0	5	5	0	5	5	0	5	0	0	0	0	0	0
OC-	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na
8	2	2	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	1	2	1	0	1	0
1-	2	2	2	2	1	1	1	1	1	1	2	0	1	1	1	1	1	1	2	0	0	0	0	0
-	1	1	1	1	1	1	1	1	1	1	3	0	1	1	1	1	1	1	3	0	1	0	0	1
)x2	10	10	10	10	6	8	8	8	8	8	14	2	8	8	8	8	8	14	2	2	2	2	2	2
b+C	35	35	35	35	30	6	33	33	33	33	39	2	33	33	33	33	33	33	33	33	34	2	2	2
0)																								

Reizwert: Ø18 = 28

KLÄRUNG siehe letzte Seite

Bemerkungen: näßig reizend

Gelbk. Gelbk.
Dr.med.habil.Dr.rer.nat. Gelbk.

ZEICHENERKLÄRUNG/HAUTREIZWIRKUNG

Rötung: 1 = fraglich, 2 = leicht, 3 = stark, 4 = sehr stark;
Ödem: 1 = sehr leicht; 2 = leicht; 3 = stark; 4 = sehr stark;
S = Schuppenbildung, sS = starke Schuppenbildung;
N = Nekrose (w = weich, p = pergamentartig, l = lederartig,
h = hart verschieblich, t = tiefgehend; fl = fleckig nekrotisch);
Na = Narben; ü = übergreifend; id = induriert;

ZEICHENERKLÄRUNG/SCHLEIMHAUTREIZWIRKUNG:

Zu A und 3 B: Intensität der Symptome:

1 = leicht; 2 = deutlich; 3 = stark; 4 = sehr stark;

Zu 1 B: Betroffene Fläche: 1 \leq 1/4; 2 \geq 1/4 aber < 1/2;
3 \geq 1/2 aber < 3/4; 4 \geq 3/4;

Zu 2.: 1 = ziliare Injektion; 2 = Iritis;

Zu 3 A und 3 C: Intensität der Symptome:

1 = leicht; 2 = deutlich; 3 = stark;

Na = Narbe; E = Eiterung; H = Haarausfall; V = Verätzung, St =
Staphylom; HA = Hornhautablösung; N = Nickhaut; S = Schleimhaut;
w = weiß; g = grau; rb = rotbraun; B = Blut; eG = einwachsende
Gefäße; Pv = Pupille verengt

BASF

79/336

Gewerbehygiene und
Toxikologie

18.02.80, dd

Sanitized Copy

G E W E R B E T O X I K O L O G I S C H E G R U N D P R Ü F U N G

Substanz-Nr.: 79/336
Ihr Schreiben vom: -
Auftrag vom: 21.05.79
Eingang: 22.05.79

COMPANY SANITIZED

Produkt: Hydraulan DOT 4/H 402
(flüssig)

Chemische Bezeichnung (Formel, Zusammensetzung):

Tl. Methyltetraglykol

Substanz: Hydraulan DOT 4/H 402
Substanz-Nr.: 79/336

ERGEBNIS DER GEWERBETOXIKOLOGISCHEN GRUNDPRÜFUNG

ANGABEN ZUR TOXIZITÄT

1. AKUTE ORALE TOXIZITÄT (Ratte):
 $LD_{50} > 5000 \text{ mg/kg}$.

2. AKUTES INHALATIONSRISIKO (Ratte; Testergebnis abhängig von Toxizität UND Flüchtigkeit/Staubentwicklung; Rückschlüsse auf die akute Inhalationstoxizität sind nicht möglich; Methodik gemäß (4)):

Nach 7 Stunden Exposition in einer bei 20 °C angereicherten Atmosphäre keine Tiere gestorben.

3. PRIMÄRE HAUTREIZWIRKUNG (Kaninchen; BASF- und Draize-Test in Anlehnung an (5)):

Primärer Reizwert: ca. 5 (vgl. 5)

Bewertung: mäßig reizend bei langdauernder Einwirkung

Die Veränderungen traten erst nach längerer Einwirkungsdauer auf. Die Reizerscheinungen bildeten sich innerhalb von 8 Tagen an der intakten Haut unter Krustenbildung überwiegend zurück, dagegen entstanden an der skarifizierten Haut teilweise oberflächliche Gewebsdefekte (Nekrosen).

4. PRIMÄRE SCHLEIMHAUTREIZWIRKUNG (Kaninchenauge; Draize-Test in Anlehnung an (5)):

Primärer Reizwert: ca. 37 (vgl. 5)

Bewertung: mäßig reizend

Bei Einwirkung der Substanz auf die Augen muß mit HORNHAUTTRÜBUNGEN und ENTZÜNDUNGEN AN DER REGENBOGENHAUT gerechnet werden.

Die pathologischen Befunde am Auge und die Reizerscheinungen an der Schleimhaut bildeten sich innerhalb von 15 Tagen weitgehend zurück.

VORSCHLÄGE ZUR KENNZEICHNUNG

1. Gefahrenhinweise

Substanz: Hydraulan DOT 4/H 402
Substanz-Nr.: 79/336

2. Sicherheitsratschläge

S 25 = Berührung mit den Augen vermeiden (gemäß (1))

Länger dauernde Berührung mit der Haut vermeiden.

Im übrigen sind die beim Umgang mit Chemikalien üblichen Vorsichtsmaßregeln zu beachten.

3. Gefahrensymbol (gemäß (1)) reizend = Xi

4. Kennzeichnung für den Transport (gemäß (3)): nicht erforderlich

Die Vorschläge zur Kennzeichnung stützen sich allein auf die Haut- und Schleimhautreizwirkung und die orale Toxizität.

BESONDERE BEMERKUNGEN

Die Ergebnisse des Inhalations-Risiko-Testes kennzeichnen eine Gefahr, die sich durch Einatmen der Substanz ergeben kann. Die Zuordnung einer akuten toxischen Wirkung (sehr giftig - gesundheitsschädlich) durch Einatmen mit den entsprechenden R- und S-Sätzen ist durch die Ergebnisse des Testes allein nicht möglich. Hierzu ist die Durchführung eines akuten Inhalations-Toxizitäts-Testes (LC_{50}) erforderlich.

(1) Nach EG-Richtlinien (27.06.67 und 14.07.76)

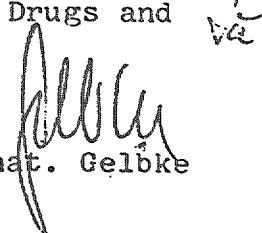
(3) Nach UNO-Empfehlungen (Transport of Dangerous Goods, UN, New York, 1977)

(4) In Anlehnung an H.F. Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95 - 107 (1962)

(5) Federal Register 38, No. 187, § 1500.41 (Haut) und § 1500.42 (Auge), S. 27019 vom 27.09.73.

Bewertung nach: Draize, J.H. (1959): Dermal Toxicity. In: FDA-Appraisal of the Safety of the Chemicals in Foods, Drugs and Cosmetics.


Dr. med. Hofmann


Dr. med. habil. Dr. rer. nat. Gelbke

AKUTE TOXIZITAET

SUBSTANZ NUMMER	79 / 336	
SUBSTANZBEZ.	HYDRAULAN DOT 4/ H 402	
ZUBEREITUNG MIT	AQUA DEST.	
APPLIKATIONSFORM	EMULSION	
APPLIKATIONSART	ORAL	
TIERART	RATTE/SPRAGUE/DAWLEY/HAGEMANN	
FUTTER	HERILAN MRH-HALTUNG; H. EGGERSMANN KG	
NUECHTERNPERIODE	15H - 20H VOR APPL.	
BEOBACHTUNGSDAUER	14 D	
DATUM DER APPL.	13. 7.79	
DOSIS	MG/KG	5000
KOHZ. %	(G/V)	50
APPL.VOL.	ML/KG	10

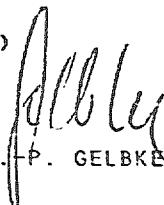
ERGEBNIS

LD50 NACH 14 D

M+W : GROESSER 5000 (MG/KG) < 1 % SIGNIFIKANZLEVEL

VERSUCHSDURCHFUEHRUNG : DR. MED. HABIL. DR. RER. NAT. H.-P. GELBEK

SYMBOLE : D = "TAG" ; H = "STUNDE"
 M = MAENNLICH ; W = WEIBLICH



51145

79 / 336 RATTE / P.O.

BLATT 2

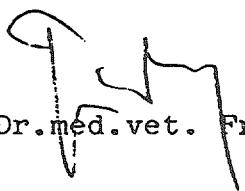
A K U T E T O X I Z I T A E T
=====

SYMPTOME :

DOSIS	MG/KG	5000
HAUTROETUNG		***

SEKTIONSBEFUNDE:

Getötete Tiere: Organe o.B.


Dr. med. vet. Freisberg

SYMBOLE : *** = SYMPTOM VORHANDEN

79 / 336 RATTE / P.O.

BLATT 3

AKUTE TOXIZITAET
=====

DOSIS	MG/KG	5000
-------	-------	------

MORTALITAET:

ANZAHL DER TIERE	M	5
TOTE TIERE NACH		
1 H	0	
1 D	0	
2 D	0	
7 D	0	
14 D	0	

ANZAHL DER TIERE	W	5
TOTE TIERE NACH		
1 H	0	
1 D	0	
2 D	0	
7 D	0	
14 D	0	

MITTELGEW. (G):

VERSUCHSBEGINN	M	220
NACH:		
2- 4D	256	
7 D	281	
13 D	308	

VERSUCHSBEGINN	W	170
NACH:		
2- 4D	194	
7 D	204	
13 D	204	

SYMBOLE : D = "TAG" ; H = "STUNDE"
 M = MAENNLICH ; W = WEIBLICH

79 / 336 RATTE / P.O.

BLATT 4

A K U T E T O X I Z I T A E T
=====

LD50-BESTIMMUNG : BEOBSACHTUNGSDAUER 14 D
TIERE MAENNLICH UND WEIBLICH

DOSEN (MG/KG)	ANZAHL TIERE	TOTE NACH 14 D	MORTA- LITAET (%)	DOSEN VER- WENDET
5000	10	0	0.	*

LD50-WERT > 5000 (1 % SIGNIFIKANZLEVEL)

24.8.79

Pi@

Substanz: Hydraulan DOT 4/H 402
 Substanz-Nr.: 79/336

AKUTES INHALATIONSRISIKO - Inhalations-Risiko-Test (Ratte; in Anlehnung an H.F. Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107 (1962))

Inhalation einer bei ~~RÄUMMEMPENNSKIN~~ 20°C durch das Produkt geleiteten Atmosphäre. Es werden zur Anreicherung 200 l Luft/h durch eine 5 cm hohe Schicht des Produktes geleitet.

Mortalität x/y gestorbene/exponierte Tiere

Expositionszeit	3'	10'	30'	1 h	3 h	h
Dampf						
flüchtige Anteile						
möglicherweise flüchtige Anteile						0/12
Staub						

SYMPTOME:

keine

Klimisch
 Dr.rer.nat. Klimisch

SEKTIONSBEFUNDE:

Getötete Tiere: Organe o.B.

T
 Dr.med.vet. Freisberg

Substanz: Hydraulan DOT 4/II 402
 Substanz-Nr.: 79/336

AKUTES INHALATIONSRISIKO - Inhalations-Risiko-Test (Ratte; in Anlehnung an H.F. Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107 (1962))

Inhalation einer bei RÄUMTEMPERATUR 20°C durch das Produkt geleiteten Atmosphäre. Es werden zur Anreicherung 200 l Luft/h durch eine 5 cm hohe Schicht des Produktes geleitet.

Mortalität x/y gestorbene/exponierte Tiere

Expositionszeit	3'	10'	30'	1 h	3 h	h
Dampf						
flüchtige Anteile						
möglicherweise flüchtige Anteile						0/12
Staub						

SYMPTOME:

keine

Klimisch
.....
Dr.rer.nat. Klimisch

SEKTIONSBEFUNDE:

Getötete Tiere: Organe o.B.

T
.....
Dr.med.vet. Freisberg

Substanz: Hydraulan DOT 4/H 402
Substanz-Nr.: 79/336

4stündiger Test auf Ätzwirkung am Kaninchen

Applikationsform: unverändert

Tier Nr.	4 Stunden		1 Tag		2 Tage		8 Tage	
	Rötung	Ödem	Rötung	Ödem	Rötung	Ödem	Rötung	Ödem
1	0	0	0	0	0	0	0	0
2	0	0	1	0	0	0	0	0

ZEICHENERKLÄRUNG

Rötung: 1 = fraglich

Dr. rer. nat. Grundler

Versuchsdurchführung:

HAUTREIZNIRKUNG (FED. REG.)

=====

SUBSTANZ NUMMER	79 / 336
SUBSTANZBEZEICH.	HYDRAULAN DOT 4/H 402
APPLIKATIONSFORM	UNVERAENDERT
APPLIKATIONSMENGE	CA. 0.5 ML AUF 2.5 CM X 2.5 CM
TIERART	KANINCHEN/WEISSE WIENER (GAUKLER)
FUTTER	SSNIFF DER FIRMA INTERMAST
BEZOCHTUNGSDAUER	8 D
TIERANZAHL M	1
	W 2
MITTELGEW. (KG) M	2.32
	W 2.57
APPLIKATIONSDATUM	2. 7.79

ERGEBNIS (*): PRIMAERER REIZWERT CIRKA 5.0
===== AUFGRUND DES PRIMAEREN REIZWERTES IST DIE SUBSTANZ
ALS "MAESSIG REIZEND" ZU BEZEICHNEN.

DER PRIMAERE REIZWERT LIESS SICH NICHT GENAU BERECHNEN, DA
EINE EXAKTE BEFUNDERHEBUNG NICHT IN ALLEN FAELLEN MOEGLICH WAR.

VERSUCHSDURCHFUEHRUNG : DR. RER. NAT. O.J. GRUNDLER

SYMBOLE: M = MAENNICH
W = WEIBLICH
D = TAG

* METHODE IN ANLEHNUNG AN FEDERAL REGISTER 38, NO. 187,
PARA. 1500.41, S. 27029 VOM 27.09.73

HAUTREIZWIRKUNG (FED. REG.)

=====

TIERNUMMER	0.775	0.733	0.703	
TIERGEW.(KG)	2.51	2.64	2.32	
GESCHLECHT	WEIBL.	WEIBL.	MAENNL.	
				MW
HAUTREZTUNG				
INTAKT 24 H	2	2 R:U/O:U	2	2.0
72 H	4	2	2	2.7
N:P				
8 D	4 N:E/+	K K/+	K K/+	
SKARI- FIZIERT 24 H	3 R:U/O:U	3 R:U/O:U	2 R:U/O:U	2.7
72 H	4 O:U	4 N:P	4 N:P	4.0
N:P				
8 D	K K/+	4 N:X/+	4 N:X/+	
OEDEMBILDUNG				
INTAKT 24 H	2	2	2	2.0
72 H	2	2	2	2.0
8 D	1	1	1	
SKARI- FIZIERT 24 H	2	3	3	2.7
72 H	2	2	2	2.0
8 D	1	1	1	

PRIMAERER REIZWERT: CIRKA 5.0 = 1/4 *20.0

SYMBOLE: H = STUNDE

D = TAG

MW = MITTELWERT

HAUTREIZWIRKUNG (FED. REG.)

=====

ORDINALSKALA DER HAUTROETUNG UND OEDEMBILDUNG:

- 0 : KEINE
- 1 : FRAGLICH
- 2 : LEICHT
- 3 : STARK
- 4 : SEHR STARK

SIND IN EINER ZEILE BEI 1 BIS 3 TIEREN WERTE NICHT ABLESEBAR,
 SO WIRD EINMAL FUER DIE FEHLENDEN WERTE DER MINIMALE
 UND EINMAL DER MAXIMALE DER ABLESEBAREN WERTE EINGESetzt.
 (SIND MINIMUM UND MAXIMUM GLEICH, WIRD DER ABLESEBARE WERT EINGESetzt)

ZUR BERECHNUNG DES PRIMAEREN REIZWERTES WERDEN DIE NACH 24 UND 72 H
 ERHOBENEN EINZELWERTE UEBER DIE VERSUCHSTIERE GEMITTELT; DIE SUMME
 DIESER MITTELWERTE WIRD DURCH 4 GETEILT UND ERGIBT DEN PRIMAEREN REIZWERT.

SYMBOLERLAEUTERUNG:

K	- KRUSTE	
N	-- NEKROSE	
N:P	- NEKROSE	: PERCAMENTARTIG
N:E	- NEKROSE	: ERBEGROSS
N:X	- NEKROSE	: OBERFLAECHLICH
O:U	- OEDEM	: UEBERGREIFEND
R:U	- ROETUNG	: UEBERGREIFEND
+	-- BEFUND MAKROSKOPISCH PATHOLOGISCH GESICHERT	

19.10.79
38

79 / 336

BLATT 1

REIZPRUEFUNG AM AUGE (FED. REG.)
=====

SUBSTANZ NUMMER	79 / 336
SUBSTANZBEZEICH.	HYDRAULAN DOT 4/H 402
APPLIKATIONSFORM	UNVERAENDERTE
APPLIKATIONSMENGE	0.1 ML
TIERART	KANINCHEN/WEISSE WIENER (SAUKLER)
FUTTER	SSNIFF DER FIRMA INTERMAST
BEOBSACHTUNGSDAUER	15 D
TIERANZAHL	M 3 W 0
MITTELGEW. (KG)	M 2.68 W
APPLIKATIONSDATUM	2. 7.79

ERGEBNIS (*): PRIMAERER REIZWERT CIRKA 37
 ====== AUFGRUND DES PRIMAEREN REIZWERTES IST DIE SUBSTANZ
 ALS "MAESSIG REIZEND" ZU BEZEICHNEN.

G. Müller

VERSUCHSDURCHFUEHRUNG : DR. RER. NAT. O.J. GRUNDLER

SYMBOLE: M = MAENNLICH
 W = WEIBLICH
 D = TAG

* METHODE IN ANLEHNUNG AN FEDERAL REGISTER 38, NO. 187,
 PARA. 1500.42, S. 27029 VOM 27.09.73

REIZPRUEFUNG AM AUGE (FED. REG.)
=====

TIER	1	2	3				
TIERNUMMER	0.585	B1357/3..	0.805				
TIERGEW.(KG)	2.73	2.88	2.42				
GESCHLECHT	MAENNL.	MAENNL.	MAENNL.				
TIER	HORNHAUT TRUE- BUHG	IRIS FLAECHE		BINDEHAUT ROE- TUNG	SCHWEL- LUNG	SEKRE- TION	SONSTIGE
24 H 3	1 2 1	4 4 1		2 2 2	2 2 2	2 3 2	NA NA/E NA
48 H 3	1 2 1	4 4 1		2 2 2	2 2 2	2 3 2	NA/PV NA/E/PV NA
72 H 3	1 2 1	4 4 1		2 2 2	1 1 1	2 3 2	NA/PV/EG NA/E/PV NA
8 D 3	1 2 1	3 4 3		2 2 0	1 0 0	2 1 1	NA/PV/EG NA/PV NA
15 D 3	1 2 0	0 0 0		2 1 1	1 0 0	2 1 0	NA/EG NA NA

PRIMAERER REIZWERT

CIRKA 37 = 1/ 9 x 333

SYMBOLE: H = STUNDE
D = TAG

REIZPRUEFUNG AM AUGE (FED. REG.)
=====

ERLAEUTERUNGEN DER ZAHLEN:

SCHWELLUNG DER BINDEHAUT:
TRUEBUNG DER HORNHAUT:0 = NICHT VORHANDEN
1 = LEICHT
2 = DEUTLICH
3 = STARK
4 = SEHR STARKBETROFFENE FLAECHE DER
HORNHAUT:1 = > 0 ; < 1/4
2 = >= 1/4 ; < 1/2
3 = >= 1/2 ; < 3/4
4 = >= 3/4

ROETUNG DER BINDEHAUT:

0 = NORMAL
1 = LEICHT VERSTAERKT
2 = DEUTLICH
3 = STARK

SEKRETION:

0 = NORMAL
1 = LEICHT VERMEHRT
2 = DEUTLICH VERMEHRT
3 = STARK VERMEHRT

IRIS:

1 = ZILIARE INJEKTION
2 = ISTITISREIZWERTBERECHNUNG:
FUER EIN TIER:A = 5 * TRUEBUNG * FLAECHE
B = 5 * IRIS
C = 2 * (ROETUNG + SCHWELLUNG + SEKRETION)
GESAMT = A + B + CDER PRIMAERE REIZWERT IST DIE SUMME ALLER "GESAMT"-WERTE
UEBER ALLE TIERE UND DIE ZEITPUNKTE 24H, 48H, 72H
DIVIDIERT DURCH 3 * TIERANZAHL.

ERLAEUTERUNG DER BUCHSTABEN:

EG	- EINGEWACHSENE GEFAESSE
E	- EITERUNC
NA	- MARBE
PV	- PUPILLE VERENGTE

12. IX. 79
29

BASF Aktiengesellschaft
Emissionsüberwachung und Ökologie
Labor für Ökotoxikologie
Postfach
D-67056 Ludwigshafen

A b s c h l u ß b e r i c h t

Bestimmung der Hemmwirkung von
Hydraulan 401
auf die Zellvermehrung des Bakteriums *Pseudomonas putida*.

Projektnummer

93/1451/70/1

Zeitraum der Prüfung

vom 15.11.1993 bis 16.11.1993

Prüfleiter

Dr. Andreeae

Tel. 0621/60-58385 (Z 570)

TITEL

Bestimmung der Hemmwirkung von
Hydraulan 401
auf die Zellvermehrung des Bakteriums Pseudomonas putida.

ZUSAMMENFASSUNG UND DISKUSSION

Die Ergebnisse geben die Konzentrationen an eingewogenem Testgut an, die nach 16stündiger Inkubation, eine Wachstumshemmung um 10 %, 50 % bzw. 90 % im Vergleich zur Kontrolle verursachen.

EC₁₀ = 482 mg/l

EC₅₀ = 835 mg/l

EC₉₀ = 1157 mg/l

Bemerkungen : keine

Diese Untersuchung wurde nach den GLP-Prüfrichtlinien (OECD) durchgeführt. Die Archivierung aller Daten bzw. Proben wird bei der Abteilung DUU/O im Gebäude Z 570 vorgenommen.

Bearbeiter



22.11.93

Sturm

Prüfleiter


22.11.93

Dr. Andreae

Fachlicher Leiter
der Prüfeinrichtung


23.11.93

Dr. Tillmann

Auftraggeber

Hr. Pammer

BASF AG, ES/U, C 300

Inhaltsangabe

- S. 4 Gewährleistungserklärung
 - S. 5 Erklärung der Qualitätssicherungseinheit
 - S. 6 Einleitung
 - S. 7 Behandlung der Substanz
 - S. 7 Testorganismus
 - S. 7 - 8 Kultur und Testbedingungen
 - S. 9 Testparameter / Messungen
 - S. 9 Testkriterien
 - S. 10 Ergebnisse / Bemerkungen
 - Anhang 1 Meßwerte
 - Anhang 2 Graphik der Dosis-Wirkungs-Beziehung
 - Anlage Angaben des Herstellers zur Prüfsubstanz
-

GEWÄRLEISTUNGSERKLÄRUNG

Projekt-Nummer : 93/1451/70/1

Prüfsubstanz : Hydraulan 401

Prüfleiter : Dr. Andreeae
DUU/00
BASF Aktiengesellschaft
Postfach
D-67056 Ludwigshafen
Tel. 0621/60-58385

Titel : Bestimmung der Hemmwirkung von
Hydraulan 401
auf die Zellvermehrung des Bakteriums
Pseudomonas putida.

Hiermit versichere ich, daß die vorangenannte Prüfung gemäß den
OECD-Grundsätzen der Guten Laborpraxis (GLP) vom 04.02.1983, bzw.
ChemG vom 14.03.1990, Anhang 1, durchgeführt wurde.

22.11.93

Datum

H. Andreeae

Dr. Andreeae

ERKLÄRUNG DER QUALITÄTSSICHERUNGSEINHEIT

Projekt-Nummer 93/1451/70/1 QAU-Nr. 93/154

Name der Prüfsubstanz Hydraulan 401

Durchgeführte Prüfung Bestimmung der Hemmwirkung auf die Zellvermehrung des Bakteriums Pseudomonas putida

Die Qualitätssicherungseinheit hat die unten angegebenen Inspektionen durchgeführt und dem Prüfleiter sowie dem Leiter der Prüfeinrichtung darüber berichtet.

Inspektion	Inspektions-datum	Bericht an den Prüfleiter und den Leiter der Prüfeinrichtung am
Prüfplan	10.11.93	23.11.93
Durchführung der Prüfung	-	23.11.93
Abschlußbericht	23.11.93	23.11.93

Ludwigshafen, den 23.11.93

Schieck
.....
Schieck
(Qualitätssicherungseinheit)

Auftraggeber : Hr. Pammer BASF AG ES/U - C 300

Auftragsdatum : 22.06.1993

Projektnummer : 93/1451/70/1

Substanzbezeichnung : Hydraulan 401

E I N L E I T U N G

Ziel des Tests ist die Bestimmung der Wirkung einer Substanz auf das Wachstum eines grammnegativen, aeroben Bakteriums aus der Familie der Pseudomonadaceae; bewegliche Stäbchen (Durchmesser 0.7 bis 1.1 μm ; Länge 2.0 bis 4.0 μm) mit polarer Begeißelung. Es kommt ubiquitär in Boden, Wasser und Abwasser vor. Die optimale Wachstumstemperatur liegt zwischen 25 und 30° C.

Die Bakterien werden unter festgelegten Bedingungen kultiviert und die Zellvermehrung unter dem Einfluß von Testgut im Vergleich zur Kontrolle bestimmt.

Die Testdurchführung erfolgt gemäß DIN 38412 Teil 8, und den in der SOP aufgeführten allgemeinen Versuchsbedingungen.

BEHANDLUNG DER SUBSTANZ

Stammlösung : 12500 mg/l (w/v)

geprüfter Konzentrationsbereich : 10000 - 39,1 mg/l

TESTORGANISMUS

Der verwendete Teststamm von *Pseudomonas putida* DSM 50026 wird in regelmäßigen Abständen von der DSM (Deutsche Sammlung von Mikroorganismen in Göttingen) bezogen und im Labor für Ökotoxikologie der BASF AG Ludwigshafen auf Schrägagar zur Weiterzucht gehalten.

KULTUR UND TESTBEDINGUNGEN

Temperatur : 21 ± 1° C

Beleuchtung : Tag/Nacht Rhythmus

Nährlösungen : Für die Kultivierung der Bakterien werden 3 verschiedene Medien benötigt.

	Stammkultur	Vorkultur (g/l)	Testmedium
Natriumnitrat	1,0	0,5	0,5
Dikaliumhydrogenphosphat	0,24	0,12	0,12
Kaliumdihydrogenphosphat	0,12	0,06	0,06
Magnesiumsulfat heptahydrat	0,4	0,2	0,2
D(+) -Glukose	11,0	2,2	2,2
Eisencitrat	0,001	0,0005	0,0005
Hefeextrakt	0,1	0,05	----
Agar	18,0	----	----

Zur Herstellung des Mediums wird deionisiertes Wasser verwendet.

Stammkultur

Gefäß : Schrägagar-Kulturröhrchen, Nennvolumen 50 ml
Volumen : 10 ml
Animpfdichte : Impfösenausstrich
Wachstumsdauer : wöchentliche Passage

Vorkultur

Gefäß : Erlenmeyerkolben, Nennvolumen 250 ml
Volumen : 100 ml
Animpfdichte : 10 TE/F optische Dichte als Standard-Formazin-Einheit
Wachstumsdauer : ca. 7 h unter Schütteln bei $21 \pm 1^\circ\text{C}$

Testkultur

Gefäß : Penicillingläser mit abgeflachtem Boden (Nennvolumen 50 ml) und luftdurchlässigen Silikonschwammkappen.
Volumen : 10 ml
Animpfdichte : 5 TE/F
Wachstumsdauer : 16 ± 1 h unter Schütteln bei $21 \pm 1^\circ\text{C}$

Testansätze

Parallelen : 4 beimpfte Parallelen
 1 unbeimpfte Parallel
Konzentrationen : 9 Konzentrationen
Applikationsart : Flüssig-Dosierung aus einer Stammlösung

TESTPARAMETER/MESSUNGEN

Messung der optischen Dichte : Zum Zeitpunkt 16 h in allen Parallelen (Pharmazia Novaspec 2, 1 cm Küvette bei einer Wellenlänge von 436 nm)

pH-Wert-Messung : Zum Zeitpunkt t 0 in einer unbeimpften Parallelle. Zum Zeitpunkt 16 h in allen Parallelen.

TESTKRITERIEN

Testparameter ist die Vermehrungsfähigkeit der Bakterienkultur. Dazu wird die optische Dichte der Bakteriensuspension im Photometer bei 436 nm im Anschluß an die Inkubation bestimmt. Der Toxizitätsnachweis ergibt sich aus dem Vergleich der Extinktionswerte der Kontrollpopulation zu denen der behandelten Kulturen.

Neben der Darstellung der Einzelwerte werden die Mittelwerte, die Standardabweichungen und Variationskoeffizienten angegeben. Die Prozentwerte der Mittelwerte in Relation zu denen der Kontrolle (gleich 100%) veranschaulichen die Dosis-Wirkungsbeziehung der geprüften Substanz.

Die Ergebnisse geben die effektiven Konzentrationen (EC) an Testgut an, die eine Wachstumshemmung um 10 % (EC_{10}), 50 % (EC_{50}) und 90 % (EC_{90}) im Vergleich zur Kontrolle verursachen.

Die toxische Grenzkonzentration entspricht der EC 10.

Die Konzentrationsangabe zum Testgut wird immer in mg/l gemacht.

Gültigkeitskriterien:

- Wachstum des Kontrollansatzes auf mindestens das 100fache der Einstieg.
 - Variationskoeffizient der Mittelwerte < 10 %, außer bei sehr niedriger Bakteriendichte bzw. hoher Toxizität.
 - Testsubstanz im Photometer störfrei
-

Prüfbeginn : 15.11.1993

Prüfende : 16.11.1993

Ergebnisse :

EC₁₀ (16 h) = 482 mg/l

EC₅₀ (16 h) = 835 mg/l

EC₉₀ (16 h) = 1157 mg/l

Bemerkungen : keine

Pseudomonas-Zellvermehrungshemmtest DIN 38412 Teil 8

Einzelwerte und Auswertung

93/1451/70/1

Hydraulan 401

Projektnummer:

Testsubstanz:

optische Dichte bei 436 nm

Konzentration (mg/l)	16 h Pa.1	Pa.2	Pa.3	Pa.4	ub.
	0,957	0,985	0,977	0,982	0,001

Kontrolle	0,957	0,985	0,977	0,982	0,001
10000	0,031	0,032	0,047	0,032	0,020
5000	0,017	0,018	0,020	0,020	0,010
2500	0,012	0,015	0,014	0,022	0,005
1250	0,014	0,008	0,010	0,009	0,005
625	0,833	0,835	0,840	0,849	0,005
312,5	0,927	0,956	0,951	0,978	0,005
156,3	0,953	0,973	0,979	0,974	0,005
78,1	*0,037	0,952	0,968	0,970	0,005
39,1	0,949	*0,098	0,970	0,949	0,004

Konzentration (mg/l)	Statistik						Wirkung						DTI Werte						
	16 h ub.	s	v	x-ub.	%W/K	%H/K	0h ub.	16h ub.	beimpft	Pa.1	Pa.2	Pa.3	Pa.4	7,12	7,06	6,98	7,05	6,99	6,95
Kontrolle	0,975	0,01	1,29	0,974	100,0	0,0	0,0	0,0	0,0	7,12	7,06	6,98	7,05	6,99	6,95	6,95	6,95	6,95	6,95
10000	0,036	0,01	21,64	0,016	1,6	98,4	7,47	7,45	3,17	3,13	3,14	2,73							
5000	0,019	0,00	8,00	0,009	0,9	99,1	7,33	7,32	7,16	7,16	7,15	7,15							
2500	0,016	0,00	27,61	0,011	1,1	98,9	7,22	7,23	7,05	7,06	7,06	7,05							
1250	0,010	0,00	25,66	0,005	0,5	99,5	7,16	7,13	6,91	6,97	6,96	6,97							
625	0,839	0,01	0,834	85,6	14,4	7,13	7,10	6,48	6,61	6,57	6,56	6,56							
312,5	0,953	0,02	2,20	0,948	97,3	2,7	7,11	7,11	7,08	7,10	7,15	7,15							
156,3	0,970	0,01	1,18	0,965	99,0	1,0	7,10	7,11	7,02	7,15	7,16	7,18							
78,1	0,963	0,01	1,02	0,958	98,4	1,6	7,10	7,11	*3,97	7,10	7,17	7,16							
39,1	0,956	0,01	1,27	0,952	97,7	2,3	7,10	7,07	7,07	*3,95	7,11	7,10							

Abkürzungen:

Pa.
ub.

Parallele
unbeimpft

x
Mittelwert

s
Standardabweichung

v
Variationskoeffizient

%W/K
Wert Wachstum % der Kontrolle

%H/K
Wert Hemmung % der Kontrolle

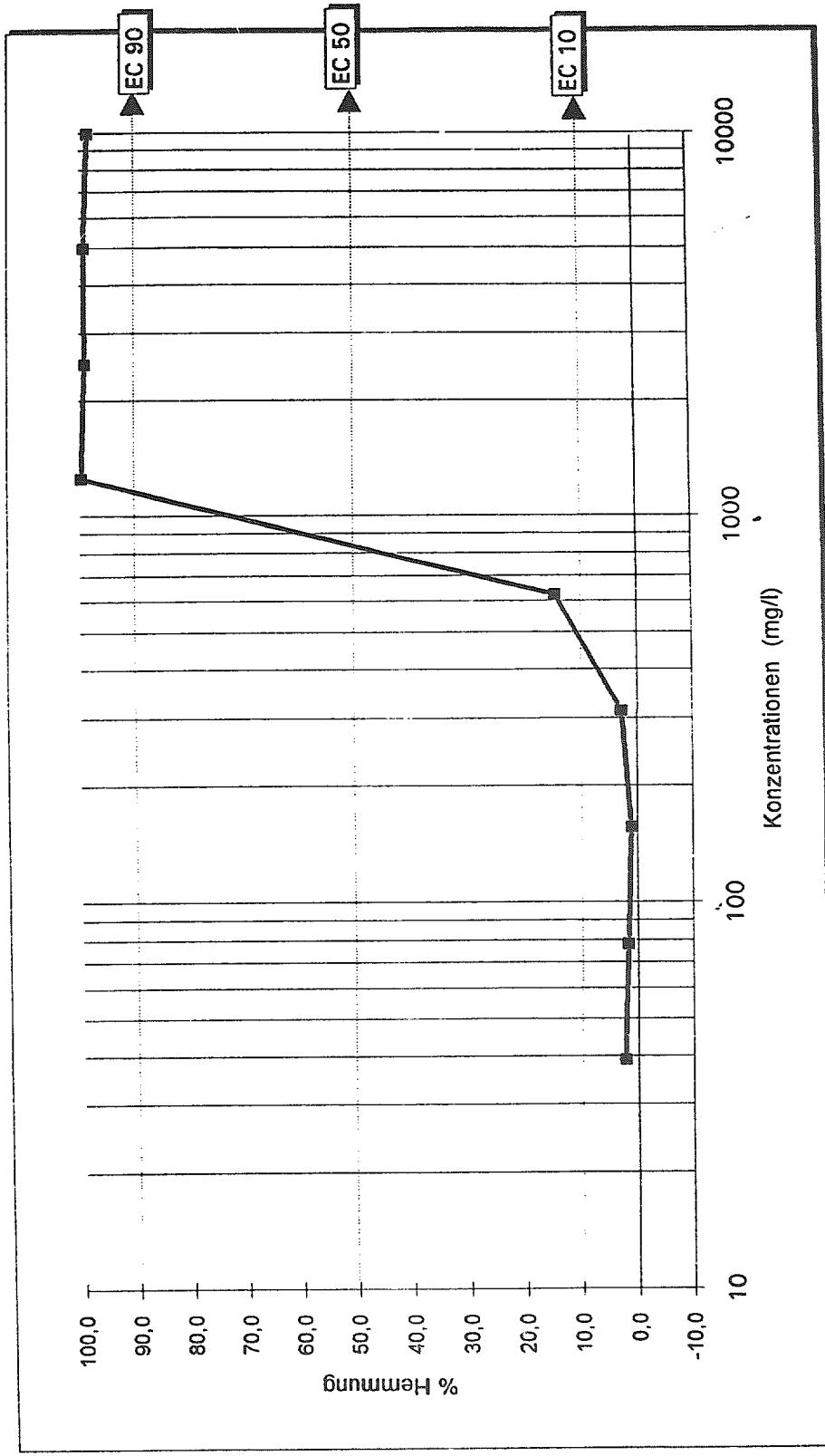
* So gekennzeichnete Werte werden
für die Auswertung nicht verwendet

Anhang 2 zum Abschlußbericht : Graphik der Dosis-Wirkungs-Beziehung

Projektnummer :
Testsubstanz :

93/1451/70/1
Hydralan 401

Pseudomonas-Zellvermehrungshemmtest (DIN 38412 Teil 8)



EC 10	=	482	mg/l
EC 50	=	835	mg/l
EC 90	=	1157	mg/l

Auftraggeber : Hr. Pammer BASF AG ES/U - C 300
Auftragsdatum : 22.06.1993
Projektnummer : 93/1451/70/1
Substanzbezeichnung : Hydraulan 401

Angaben des Herstellers zur Prüfsubstanz

Prüfsubstanz : Hydraulan 401
Chem. Bezeichnung : es liegen keine Angaben vor
Frühere Bezeichnung : es liegen keine Angaben vor
Chargen-/Lab.J.-Nr. : Partie 108
CAS-Nr. : es liegen keine Angaben vor
Produkt-Nr. : es liegen keine Angaben vor
Aggregatzustand : flüssig
Reinheitsgrad des Wirkstoffes : es liegen keine Angaben vor
Verunreinigungen/ Begleitstoffe : es liegen keine Angaben vor
Zusammensetzung : Gemisch aus Polyglykolethern, Borsäureestern von Polyglykolethern und Polyglykolen und Inhibitoren.
Homogenität : ja
Stabilität : Stabil gegenüber Temperatur, Licht, Schlag/Stoß, Luftsauerstoff, Wasser und anderen protonierten Lösemitteln; sowie gegenüber Säuren und Laugen.
Wasserlöslichkeit : ja, beliebig mischbar bis 10 g/l

Confidential

NOV 24 1987

Sanitized Copy
SHEET 1

PRJ. NO. 10A0406/871172

REPORT ON THE STUDY OF ACUTE ORAL TOXICITY

TESTING FACILITY:

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY
D-6700 LUDWIGSHAFEN/RHEIN, FRG

AIM OF THE STUDY:

ESTIMATE OF THE POTENTIAL ACUTE
HAZARD AFTER SINGLE ADMINISTRATION
(DETERMINATION OF THE LD₅₀)

PROJECT NUMBER:

10A0406/871172

NAME OF TEST SUBSTANCE:

SOLVENON PP

RESULT

LD₅₀ AFTER 14 D
MA+FE : GREATER THAN 2000 (MG/KG) (5% SIGNIFICANCE LEVEL)

Hildebrand, 12. XI. 87

DR. MED. VET. HILDEBRAND
(HEAD OF EXPERIMENTAL TOXICOLOGY)

Kirsch Nov. 12, 1987

DR. MED. VET. KIRSCH
(STUDY DIRECTOR)

* A DETAILED PRODUCT CHARACTERIZATION IS INCLUDED IN THE RAW
DATA

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NOV 24 1987

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SHEET 1

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REPORT ON THE STUDY OF ACUTE ORAL TOXICITY

TESTING FACILITY:

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY
D-6700 LUDWIGSHAFEN/RHEIN, FRG

AIM OF THE STUDY:

ESTIMATE OF THE POTENTIAL ACUTE
HAZARD AFTER SINGLE ADMINISTRATION
(DETERMINATION OF THE LD50)

PROJECT NUMBER:

10A0406/871172

NAME OF TEST SUBSTANCE:

SOLVENON PP

RESULT

LD50 AFTER 14 D
MA+FE : GREATER THAN 2000 (MG/KG) (5% SIGNIFICANCE LEVEL)

Hildebrand, 12.11.87

DR. MED. VET. HILDEBRAND

(HEAD OF EXPERIMENTAL TOXICOLOGY)

Kirsch Nov. 12, 1987

DR. MED. VET. KIRSCH

(STUDY DIRECTOR)

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FORM EXCEPT WITH THE PROPRIETOR'S EXPLICIT PERMISSION.

ACUTE ORAL TOXICITY

TEST METHOD:

ANIMAL SPECIES:

RAT/WISTAR/DR. THOMAE

ANIMAL BREEDER:

DR. K. THOMAE GMBH, D-7950 BIBERACH, FRG

ACCLIMATIZATION PERIOD:

ACCLIMATIZATION FOR AT LEAST 1 WEEK

NO. OF ANIMALS PER DOSE:

5 MALE ANIMALS
5 FEMALE ANIMALS

TYPE OF CAGE:

STAINLESS STEEL WIRE MESH CAGES,
TYPE DK-III (BECKER & CO.,
CASTROP-RAUXEL, FRG)

NO. OF ANIMALS PER CAGE:

5

ANIMAL IDENTIFICATION:

IDENTIFICATION OF GROUPS USING
CAGE CARDSROOM TEMPERATURE/
RELATIVE HUMIDITY:THE ANIMALS WERE HOUSED IN FULLY
AIR-CONDITIONED ROOMS. CENTRAL
AIR-CONDITIONING GUARANTEED A
RANGE OF 20 - 24 DEGREES CELSIUS
FOR TEMPERATURE AND OF 30 - 70%
FOR RELATIVE HUMIDITY. THERE
WERE NO DEVIATIONS FROM THESE
RANGES WHICH INFLUENCED THE RE-
SULTS OF THE STUDY.

DAY/NIGHT RHYTHM:

12 H/12 H (6.00 - 18.00 HOURS/
18.00 - 6.00 HOURS)

DRINKING WATER:

TAP WATER AD LIBITUM PER
DAY

DIET:

KLIBA-LABORDIAET 343, KLINGENTALMUEHLE AG
CH-4303 KAISERAUGST, SWITZERLAND,
AD LIBITUM

ANIMAL WEIGHTS:

ANIMALS OF COMPARABLE WEIGHT;
(+- 20 % OF THE MEAN WEIGHT);
FOR WEIGHING DATA SEE SHEET 5.

ACUTE ORAL TOXICITY

RESULTS:

SYMPTOMS MALE ANIMALS:

DOSE (MG/KG)	2000	1000
DYSPNEA	30M- 4H	15M- 4H
APATHY	30M- 4H	15M- 4H
ABNORMAL POSITION	30M- 4H	
STAGGERING	2H- 4H	
ATONIA	30M- 4H	
PARESIS	30M- 4H	
PAIN REFLEX ABSENT	2H- 4H	
CORNEAL REFL. ABS.	2H- 4H	
NARCOT.-LIKE STATE	2H- 4H	
PILOERCTION	30M- 1D	
EXSICCOSIS	2H- 4H	
POOR GENERAL STATE	30M- 4H	15M- 4H

SYMPTOMS FEMALE ANIMALS:

DOSE (MG/KG)	2000	1000
DYSPNEA	30M- 1D	15M- 4H
APATHY	30M- 1D	15M- 4H
ABNORMAL POSITION	30M- 4H	
STAGGERING	2H- 1D	
ATONIA	30M- 4H	
PARESIS	30M- 4H	
PAIN REFLEX ABSENT	2H- 4H	
CORNEAL REFL. ABS.	2H- 4H	
NARCOT.-LIKE STATE	2H- 4H	
PILOERCTION	2H- 1D	
EXSICCOSIS	2H- 4H	
POOR GENERAL STATE	30M- 1D	15M- 4H

Sanitized Copy**ACUTE ORAL TOXICITY**

FASTING PERIOD: THE ANIMALS WERE GIVEN NO FEED ABOUT 16 HOURS BEFORE ADMINISTRATION, BUT WATER WAS AVAILABLE AD LIBITUM.

ROUTE OF ADMINISTRATION: SINGLE ORAL ADMINISTRATION BY GAVAGE

TEST SUBSTANCE FORMULATION WITH: OLIVE OIL

REASON FOR THE VEHICLE: TEST SUBSTANCE IS INSOLUBLE IN WATER

FORM OF ADMINISTRATION: SOLUTION

AMOUNTS ADMINISTERED:

DOSE (MG/KG)	:	2000	:	1000	:	
CONC. (W/V)	:	40	:	20	:	
ADM. VOL. (ML/KG)	:	5	:	5	:	

TIME OF DAY OF ADMINISTRATION: IN THE MORNING

OBSERVATION PERIOD: 14 D

DATE OF FIRST ADMINISTRATION: SEP. 9, 87

DATE OF LAST ADMINISTRATION: OCT. 6, 87

SIGNS AND SYMPTOMS: RECORDING OF SIGNS AND SYMPTOMS SEVERAL TIMES ON THE DAY OF ADMINISTRATION, AT LEAST ONCE EACH WORKDAY. CHECK FOR MORIBUND AND DEAD ANIMALS TWICE EACH WORKDAY AND ONCE ON HOLIDAYS. FOR DATA SEE SHEETS 4 AND 5.

PATHOLOGY: WITHDRAWAL OF FOOD ABOUT 16 HOURS BEFORE SACRIFICE WITH CO₂; THEN NECROPSY WITH GROSS-PATHOLOGICAL EXAMINATION. NECROPSY OF ALL ANIMALS THAT DIE AS EARLY AS POSSIBLE.

STORAGE OF THE REPORT AND RAW DATA: ON COMPLETION OF THE REPORT ALL RAW DATA, STUDY DOCUMENTS AND THE REPORT ARE RETAINED AT BASF AKTIENGESELLSCHAFT.

DATA INPUT: REINFRANK

DATA CONTROL: *Benz, Oct. 26, 1987*

ACUTE ORAL TOXICITY

LD₅₀ DETERMINATION : OBSERVATION PERIOD 14 D
ANIMALS MALE AND FEMALE

DOSES (MG/KG)	NUMBER OF ANIMALS	DEAD ANIMALS AFTER 14 D	MORTAL- ITY (%)	DOSES USED FOR CALCULATION
1000	10	0	0.0	
2000	10	1	10.0	*

LD₅₀ > 2000 (5% SIGNIFICANCE LEVEL)

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PRJ. NO. 10A0406/871172

SHEET 5

ACUTE ORAL TOXICITY

DOSE (MG/KG) : 2000 : 1000 :

MORTALITY:

MA:		
NO. OF ANIMALS:	5	5
DEAD ANIMALS AFTER:		
1 H	0	0
1 D	1	0
2 D	1	0
7 D	1	0
14 D	1	0

FE:		
NO. OF ANIMALS:	5	5
DEAD ANIMALS AFTER:		
1 H	0	0
1 D	0	0
2 D	0	0
7 D	0	0
14 D	0	0

MEAN WEIGHT (G):

MA:		
BEG. OF THE TEST:	209	180
AFTER:		
7 D	260	244
13 D	287	280

FE:		
BEG. OF THE TEST:	203	179
AFTER:		
7 D	221	210
13 D	227	222

KEY: W/V = WEIGHT/VOLUME

MA = MALE

FE = FEMALE

D = DAY

H = HOUR

M = MINUTE

BEG. = BEGINNING

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PRJ. NO. 10A0406/871172

SHEET 7

ACUTE ORAL TOXICITY

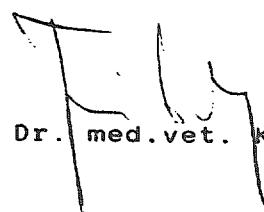
Animals that died (1 male animal):

General congestion.

Sacrificed animals (males and females):

No pathologic findings noted.

PATHOLOGY

 Oct. 28, 1987
Dr. med.vet. K.O. Freisberg

db: 1596-40

BASF
Abteilung Toxikologie
Department of Toxicology

Project No.: 18H0634/902206

Sanitized Copy

GLP STATEMENT

Title: Report on the acute dermal irritation/corrosivity
to the intact dorsal skin of
Protectol PP
in white rabbits

This study was conducted in accordance with "OECD Principles of Good
Laboratory Practice" (Paris, 1981).

Mohamed 18.6.91
Head of Experimental Toxicology

Kiraly Feb. 8, 1991
Study director

Confidential

FEB 21 1991

PRJ. NO. 18H0634/902206

SHEET 1

REPORT ON THE ACUTE DERMAL IRRITATION/CORROSIVITY TO THE INTACT
DORSAL SKIN OF THE WHITE RABBIT BASED ON OECD *

Sanitized Copy

TESTING FACILITY:

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY
D-6700 LUDWIGSHAFEN / RHEIN, FRG

AIM OF THE STUDY:

ASSESSMENT OF A POSSIBLE IRRITA-
TING OR CORROSIVE POTENTIAL TO
THE SKIN

PROJECT NUMBER:

18H0634/902206

NAME OF TEST SUBSTANCE:

PROTECTOL PP

LOT NUMBER/ DATE OF MANUFACTURING:

P. 70-1840 / JULY 14, 1990

DEGREE OF PURITY:

84.8 AREA-% 1-PHOXY-PROPAN-2-OL AND

PHYSICAL STATE/APPEARANCE:

LIQUID, ACHROMATIC

HOMOGENEITY:

THE SAMPLE APPEARED TO BE HOMOGENEOUS

STORAGE STABILITY
AT ROOM TEMPERATURE:

ON COMPLETION OF ALL TESTS THE STABILITY
OF THE TEST SUBSTANCE WILL BE VERIFIED
BY A REPEATED ANALYSIS. THE RESULT CAN
BE OBTAINED FROM THE SPONSOR (BASF AG).

CONDUCT OF ANALYTICS:

ANALYTICAL LABORATORY OF BASF AG

STORAGE CONDITIONS:

ROOM TEMPERATURE

Hildebrand, 18.6.81
DR. MED. VET. HILDEBRAND
(HEAD OF EXPERIMENTAL TOXICOLOGY)

Kirsch Feb. 8, 1991
DR. MED. VET. KIRSCH
(STUDY DIRECTOR)

* METHOD AND ASSESSMENT BASED ON OECD GUIDELINE (404) FOR
TESTING OF CHEMICALS ADOPTED MAY 12TH, 1981

** DETAILED INFORMATION ON THE CHARACTERIZATION OF THE TEST SUBSTANCE
IS INCLUDED IN THE RAW DATA

THIS REPORT IS THE PROPERTY OF BASF AKTIENGESELLSCHAFT AND MAY NOT
BE COMMUNICATED TO THIRD PERSONS, REPRODUCED, OR PUBLISHED IN ANY
FORM EXCEPT WITH THE PROPRIETOR'S EXPLICIT PERMISSION.

THIS REPORT CONSISTS OF 7 PAGES.

ACUTE SKIN IRRITATION/CORROSIVITY (OECD)

METHOD

ANIMAL SPECIES: RABBIT/WHITE VIENNA
ANIMAL BREEDER: GAUKLER: D-6050 OFFENBACH/MAIN, FRG
TYPE OF CAGE: CAGE MADE OF STAINLESS STEEL
WITH WIRE MESH WALK FLOORS,
FLOOR AREA: 40 CM X 51 CM
NO. OF ANIMALS PER CAGE: 1
ANIMAL IDENTIFICATION: EAR TATTOO (= ANIMAL NO.)
ROOM TEMPERATURE/
RELATIVE HUMIDITY: THE ANIMALS WERE HOUSED IN FULLY
AIR-CODENITIONED ROOMS. CENTRAL
AIR-CODENITIONING GUARANTEED A
RANGE OF 20 - 24 DEGREES CELSIUS
FOR TEMPERATURE AND OF 30 - 70%
FOR RELATIVE HUMIDITY. THERE
WERE NO DEVIATIONS FROM THESE
RANGES WHICH INFLUENCED THE RE-
SULTS OF THE STUDY.
DAY/NIGHT RHYTHM: 12 H/12 H (6.00 - 18.00 HOURS/
18.00 - 6.00 HOURS)
BEDDING: NO BEDDING IN THE CAGES; SAW-
DUST IN THE WASTE TRAYS
DIET: KLIBA 341, 4 MM;
FIRMA KLINGENTALMUEHLE AG
CH-4303 KAISERAUGST, SWITZERLAND
(ABOUT 130 G PER ANIMAL PER DAY)
FEED ANALYSIS: THE FEED USED IN THE STUDY WAS AS-
SAYED FOR CONTAMINANTS. IN VIEW OF
THE AIM AND DURATION OF THE STUDY
THE CONTAMINANTS OCCURRING IN COM-
MERCIAL FEED OUGHT NOT TO INFLUENCE
THE RESULTS.
DRINKING WATER: ABOUT 250 ML TAP WATER PER
ANIMAL PER DAY
DRINKING WATER ANALYSIS: THE DRINKING WATER IS REGULARLY ASSAYED
FOR CONTAMINANTS BY THE MUNICIPAL
AUTHORITIES OF FRANKENTHAL AND THE
TECHNICAL SERVICES OF BASF AKTIENGE-
SELLSCHAFT. IN VIEW OF THE AIM AND
DURATION OF THE STUDY THERE ARE NO
SPECIAL REQUIREMENTS EXCEEDING THE
SPECIFICATIONS OF THE DRINKING WATER.
ACCLIMATIZATION PERIOD: AT LEAST 8 DAYS BEFORE THE BEGINNING
OF THE STUDY: SAME HOUSING
CONDITIONS AS DURING THE STUDY
CLIPPING OF THE FUR: AT LEAST 15 HOURS BEFORE THE
BEGINNING OF THE STUDY

PRJ. NO. 18H0634/902206

ACUTE SKIN IRRITATION/CORROSIVITY (OECD)

WEIGHT DETERMINATION: SHORTLY BEFORE APPLICATION OF THE TEST SUBSTANCE

EXPOSURE PERIOD: 4 H SEMIOPCLOSIVE *

NUMBER OF ANIMALS MA: 2

FE: 1

MEAN WEIGHT (KG) MA: 2.54

FE: 2.79

APPLICATION AREA: 2.5 CM X 2.5 CM

FORM OF APPLICATION: UNCHANGED

APPLICATION VOLUME: APPLICATION OF 0,5 ML OF THE UNDILUTED TEST SUBSTANCE TO THE TEST PATCH (2,5 CM X 2,5 CM)

APPLICATION SITE: UPPER THIRD OF THE BACK OR FLANKS

REMOVAL OF THE TEST SUBSTANCE: AT THE END OF THE EXPOSURE PERIOD WITH LUTROL AND LUTROL/WATER (1:1)

OBSERVATION PERIOD: 72 H

READINGS: 30 - 60 MINUTES AFTER REMOVAL OF THE TEST PATCHES AND 24 H, 48 H, 72 H, AFTER THE BEGINNING OF APPLICATION

NEGATIVE CONTROL: UNTREATED SKIN SITES OF THE SAME ANIMAL

* TEST PATCHES WERE SECURED IN POSITION WITH A POROUS DRESSING (FOUR LAYERS OF ABSORBENT GAUZE + POROUS BANDAGE).

ACUTE SKIN IRRITATION/CORROSIVITY (OECD)

RETENTION OF RECORDS:

THE RAW DATA AS WELL AS THE
ORIGINAL OF THE PROTOCOL AND
THIS REPORT, ARE RETAINED AT
BASF AKTIENGESELLSCHAFT AT LEAST
FOR THE PERIOD OF TIME SPECIFIED
IN THE GLP-REGULATIONS.

DATA INPUT:

REINFRANK

DATA CONTROL:

Benz, Jan. 07, 91

DATE OF APPLICATION:

DEC. 10, 90

RESULTS ACUTE SKIN IRRITATION/CORROSIVITY (OECD)

ANIMAL	1	2	3
ANIMAL NO.	0190	0191	0193
A. WEIGHT (KG)	2.47	2.61	2.79
SEX	MA	MA	FE

READ- INGS	ANI- MAL	INTACT SKIN	SYMPTOMS
---------------	-------------	-------------	----------

4 H	1	0	0
-----	---	---	---

	2	1	0
--	---	---	---

	3	0	0
--	---	---	---

24 H	1	0	0
------	---	---	---

	2	0	0
--	---	---	---

	3	0	0
--	---	---	---

48 H	1	0	0
------	---	---	---

	2	0	0
--	---	---	---

	3	0	0
--	---	---	---

72 H	1	0	0
------	---	---	---

	2	0	0
--	---	---	---

	3	0	0
--	---	---	---

ME	1	0.0	0.0
----	---	-----	-----

ME	2	0.0	0.0
----	---	-----	-----

ME	3	0.0	0.0
----	---	-----	-----

ME		0.0	0.0
----	--	-----	-----

RESULTS ACUTE SKIN IRRITATION/CORROSIVITY (OECD)

EVALUATION OF ERYTHEMA (R) AND EDEMA (ED):

0 = NONE
1 = VERY SLIGHT
2 = WELL-DEFINED
3 = MODERATE TO SEVERE
4 = SEVERE TO VERY SEVERE

CALCULATION OF THE MEAN ACCORDING TO 83/467/EEC CRITERIA OF JULY 29TH, 1983
(FOR CALCULATION OF THE MEANS OF ERYTHEMA AND EDEMA ONLY THE READINGS OF 24, 48 AND 72 HOURS ARE USED).

KEY: MA = MALE
FE = FEMALE
H = HOUR
ME = MEAN

STATEMENT
OF THE QUALITY ASSURANCE UNIT

Number of test substance: 90/634

Name of test substance: Protectol PP

Title: Report on the acute dermal irritation/
 corrosivity to the intact dorsal skin of
 the white rabbit
 based on OECD

The Quality Assurance Unit performed the inspections given below,
 and reported findings to the Study Director and to Management. The
 conduct of this short-term study was not inspected; the processes
 of the laboratory and of the study involved are inspected in
 regular intervals.

Phase of study/ inspection	Date of inspection	Report to Study Di- rector and to Manage- ment
Protocol:	Dec. 7, 1990	Feb. 7, 1991
Audit of the report:	Feb. 4, 1991	Feb. 7, 1991

Remarks: The conduct of analytics was inspected independently by
 the Quality Assurance Unit of the analytical laboratory.

Ludwigshafen, Feb 20, 1991 *U. Wandelt-Hoetzl*
 U. Wandelt-Hoetzl

db; 1596-41

BASF
Abteilung Toxikologie
Department of Toxicology

Project No.: 11H0634/902207

Sanitized Copy

GLP STATEMENT

Title: Report on the acute irritation to the eye of
Protectol PP in white rabbits

This study was conducted in accordance with "OECD Principles of Good
Laboratory Practice" (Paris, 1981).

.....
Müller: 18.5.81.....
Head of Experimental Toxicology

.....
Kirsch Feb. 8, 1991.....
Study director

Confidential

FEB 21 1991

PRJ. NO. 11H0634/902207

SHEET 1

REPORT ON THE ACUTE IRRITATION TO THE EYE OF THE WHITE RABBIT
BASED ON OECD *

Sanitized Copy

TESTING FACILITY:

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY
D-6700 LUDWIGSHAFEN / RHEIN, FRG

AIM OF THE STUDY:

ASSESSMENT OF A POSSIBLE IRRITATING POTENTIAL TO THE EYE AND
TO THE EYE MUCOSA

PROJECT NUMBER:

11H0634/902207

NAME OF TEST SUBSTANCE:

PROTECTOL PP

**

LOT NUMBER/ DATE OF MANUFACTURING:

P. 70-1840 / JULY 14, 1990

DEGREE OF PURITY:

84.8 AREA-% 1-PHOENOXY-PROPAN-2-OL AND

PHYSICAL STATE/APPEARANCE:

LIQUID, ACHROMATIC

HOMOGENEITY:

THE SAMPLE APPEARED TO BE HOMOGENEOUS

STORAGE STABILITY
AT ROOM TEMPERATURE:

ON COMPLETION OF ALL TESTS THE STABILITY
OF THE TEST SUBSTANCE WILL BE VERIFIED
BY A REPEATED ANALYSIS. THE RESULT CAN
BE OBTAINED FROM THE SPONSOR (BASF AG).

CONDUCT OF ANALYTICS:

ANALYTICAL LABORATORY OF BASF AG

STORAGE CONDITIONS:

ROOM TEMPERATURE

Hildebrand. 18.5.91
DR. MED. VET. HILDEBRAND

(HEAD OF EXPERIMENTAL TOXICOLOGY)

Kirsch Feb. 8, 1991

DR. MED. VET. KIRSCH

(STUDY DIRECTOR)

* METHOD AND ASSESSMENT BASED ON OECD GUIDELINE (405) FOR TESTING OF
CHEMICALS ADOPTED MAY 12TH, 1981

** DETAILED INFORMATION ON THE CHARACTERIZATION OF THE TEST SUBSTANCE
IS INCLUDED IN THE RAW DATA

THIS REPORT IS THE PROPERTY OF BASF AKTIENGESELLSCHAFT AND MAY NOT
BE COMMUNICATED TO THIRD PERSONS, REPRODUCED, OR PUBLISHED IN ANY
FORM EXCEPT WITH THE PROPRIETOR'S EXPLICIT PERMISSION.

THIS REPORT CONSISTS OF 6 PAGES.

ACUTE EYE IRRITATION (OECD)

METHOD

ANIMAL SPECIES:

RABBIT/WHITE VIENNA

ANIMAL BREEDER:

GAUKLER; D-6050 OFFENBACH / MAIN, FRG

TYPE OF CAGE:

CAGE MADE OF STAINLESS STEEL
WITH WIRE MESH WALK FLOORS,
FLOOR AREA: 40 CM X 51 CM

NO. OF ANIMALS PER CAGE:

1

ANIMAL IDENTIFICATION:

EAR TATTOO (= ANIMAL NO.)

ROOM TEMPERATURE/
RELATIVE HUMIDITY:THE ANIMALS WERE HOUSED IN FULLY
AIR-CONDITIONED ROOMS. CENTRAL
AIR-CONDITIONING GUARANTEED A
RANGE OF 20 - 24 DEGREES CELSIUS
FOR TEMPERATURE AND OF 30 - 70%
FOR RELATIVE HUMIDITY. THERE
WERE NO DEVIATIONS FROM THESE
RANGES WHICH INFLUENCED THE RE-
SULTS OF THE STUDY.

DAY/NIGHT RHYTHM:

12 H/12 H (6.00 - 18.00 HOURS/
18.00 - 6.00 HOURS)

BEDDING:

NO BEDDING IN THE CAGES; SAW-
DUST IN THE WASTE TRAYS

DIET:

KLIBA 341, 4 MM;
FIRMA KLINGENTALMUEHLE AG
CH-4303 KAISERAUGST, SWITZERLAND
(ABOUT 130 G PER ANIMAL PER DAY)

FEED ANALYSIS:

THE FEED USED IN THE STUDY WAS AS-
SAYED FOR CONTAMINANTS. IN VIEW OF
THE AIM AND DURATION OF THE STUDY
THE CONTAMINANTS OCCURRING IN COM-
MERCIAL FEED OUGHT NOT TO INFLUENCE
THE RESULTS.

DRINKING WATER:

ABOUT 250 ML TAP WATER PER
ANIMAL PER DAY

DRINKING WATER ANALYSIS:

THE DRINKING WATER IS REGULARLY ASSAYED
FOR CONTAMINANTS BY THE MUNICIPAL
AUTHORITIES OF FRANKENTHAL AND THE
TECHNICAL SERVICES OF BASF AKTIENGE-
SELLSCHAFT. IN VIEW OF THE AIM AND
DURATION OF THE STUDY THERE ARE NO
SPECIAL REQUIREMENTS EXCEEDING THE
SPECIFICATIONS OF THE DRINKING WATER.

ACCLIMATIZATION PERIOD:

AT LEAST 8 DAYS BEFORE THE BE-
GINNING OF THE STUDY; SAME HOUSING
CONDITIONS AS DURING THE STUDY

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SHEET 3

PRJ. NO. 11H0634/902207

ACUTE EYE IRRITATION (OECD)

WEIGHT DETERMINATION: SHORTLY BEFORE APPLICATION OF THE TEST SUBSTANCE

NUMBER OF ANIMALS MA: 2

FE: 1

MEAN WEIGHT (KG) MA: 3.33

FE: 3.20

APPLICATION VOLUME: 0.1 ML (UNCHANGED)

APPLICATION SITE: SINGLE APPLICATION TO THE CONJUNCTIVAL SAC OF THE RIGHT EYELID; THE SUBSTANCE WAS NOT WASHED OUT

OBSERVATION PERIOD: 23 D

READINGS: 1 H, 24 H, 48 H, 72 H, 8 D, 17 D, 23 D.
AFTER APPLICATION

NEGATIVE CONTROL: UNTREATED EYE

RETENTION OF RECORDS: THE RAW DATA AS WELL AS THE ORIGINAL OF THE PROTOCOL AND THIS REPORT, ARE RETAINED AT BASF AKTIENGESELLSCHAFT AT LEAST FOR THE PERIOD OF TIME SPECIFIED IN THE GLP-REGULATIONS.

DATA INPUT: REINFRANK

DATA CONTROL: Benz, Jan. 07, 91

DATE OF APPLICATION: DEC. 10, 90

RESULTS ACUTE EYE IRRITATION (OECD)

ANIMAL	1	2	3
ANIMAL NO.	0130	0129	0142
A. WEIGHT(KG)	3.42	3.24	3.20
SEX	MA	MA	FE

READ- INGS	'ANI- MAL'	CORNEA		IRIS	CONJUNCTIVA		SYMPTOMS
		'OP'	'AR'		RED	SW	
1 H	1	1	3	0	2	2	3 PC/LC
	2	1	3	0	2	2	LC
	3	1	4	0	2	2	2
24 H	1	1	4	1	2	2	2 PC/S
	2	1	4	1	2	1	1
	3	1	4	1	2	1	1 PC
48 H	1	1	4	1	2	1	0
	2	1	3	0	2	0	0
	3	1	4	0	2	1	1 PC
72 H	1	1	4	0	2	1	0
	2	1	3	0	2	0	0
	3	1	4	0	2	1	1 LC/S
8 D	1	0	0	0	1	0	0
	2	1	2	0	2	0	0
	3	2	3	0	2	1	0 LC/MV
17 D	1	0	0	0	1	0	0
	2	1	2	0	2	0	0
	3	2	4	0	3	0	0 LC/PC/MV/RE
23 D	1	0	0	0	1	0	0
	2	1	2	0	2	0	1 MV/RE/S
	3	1*	1*	0*	3	0	1 MV/S/RE/S04
ME	1	1.0		0.7	2.0	1.3	
	2	1.0		0.3	2.0	0.3	
	3	1.0		0.3	2.0	1.0	
ME		1.0		0.4	2.0	0.9	

FINDINGS WHICH COULD NOT BE READ (FOR REASON SEE SYMPTOMS):

* : IF IN 1 - 2 ANIMALS ASSESSMENTS REFERRING TO THE SAME CHARACTERISTIC CANNOT BE MADE AT A PARTICULAR READING, THE MEAN ROUNDED TO THE NEAREST WHOLE NUMBER OF THE VALUES THAT CAN BE READ IS INSERTED INSTEAD.

RESULTS ACUTE EYE IRRITATION (OECD)

SCALE FOR SCORING OCULAR LESIONS:

CHEMOSIS (SW) AND CORNEA (OP)
(OPACITY-DEGREE OF DENSITY):

0 = NONE
1 = SLIGHT
2 = WELL-DEFINED
3 = SEVERE
4 = VERY SEVERE

AREA OF CORNEA INVOLVED (AR):

1 = > 0 ; < 1/4
2 = >= 1/4 ; < 1/2
3 = >= 1/2 ; < 3/4
4 = >= 3/4

CONJUNCTIVAE REDNESS (RED):

0 = NORMAL
1 = SLIGHT
2 = WELL-DEFINED
3 = SEVERE

DISCHARGE (DI):

0 = NORMAL
1 = SLIGHTLY INCREASED
2 = CLEARLY INCREASED
3 = DISTINCTLY INCREASED

IRIS:

0 = NORMAL
1 = CIRCUM-CORNEAL INJECTION
2 = IRITIS

CALCULATION OF THE MEAN ACCORDING TO 83/467/EEC CRITERIA OF JULY 29TH, 1983
(FOR CALCULATION OF THE MEANS OF OPACITY, IRIS, REDNESS AND SWELLING
ONLY THE READINGS OF 24, 48 AND 72 HOURS ARE USED).

KEY:
MA = MALE
FE = FEMALE
ME = MEAN
H = HOUR
D = DAY

EXPLANATIONS OF SYMPTOMS:

- | | |
|-----|---|
| S04 | - IRRITATION INDEX COULD NOT BE READ BECAUSE OF MARGINAL VAS- |
| | - CULARIZATION OF THE CORNEA |
| LC | - LOSS OF CORNEAL TISSUE |
| MV | - MARGINAL VASCULARIZATION OF THE CORNEA |
| PC | - PUPIL CONTRACTED |
| RE | - SMALL RETRACTIONS IN THE EYELIDS |
| S | - SUPPURATION |

**STATEMENT
OF THE QUALITY ASSURANCE UNIT**

Number of test substance: 90/634

Name of test substance: Protectol PP

Title: Report on the acute irritation to the eye of the white rabbit based on OECD

The Quality Assurance Unit inspected the study, audited the final report, and reported findings to the Study Director and to Management.

Phase of study/ inspection	Date of inspection	Report to Study Director and to Management
Protocol:	Dec. 7, 1990	Dec. 18, 1990
Conduct of study:	Dec. 18, 1990	Dec. 18, 1990
Audit of the report:	Feb. 4, 1991	Feb. 7, 1991

Remarks: The conduct of analytics was inspected independently by the Quality Assurance Unit of the analytical laboratory.

Ludwigshafen, Feb. 19, 1991

U. Wandelt-Hoetzl
 U. Wandelt-Hoetzl
 (Quality Assurance Unit)

AUG 23 1988

Confidential

PAGE 1

10F0406/875079

GOLDEN ORFE
(LEUCISCUS IDUS L., GOLDEN VARIETY)

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY

REPORT ON THE STUDY OF THE ACUTE TOXICITY

Sanitized Copy

NAME OF TEST SUBSTANCE: SOLVENON PP

ANIMAL SPECIES: GOLDEN ORFE (LEUCISCUS IDUS L., GOLDEN VARIETY)

PROJECT NO.: 10F0406/875079

SPONSOR: BASF AKTIENGESELLSCHAFT

SUMMARY AND EVALUATION:

LC 50 (MG/L; NOMINAL CONCENTRATIONS) AFTER

1H	GREATER	220	(MG/L)	(1% SIGNIFICANCE LEVEL)
	LOWER	460	(MG/L)	(1% SIGNIFICANCE LEVEL)
4H	GREATER	220	(MG/L)	(1% SIGNIFICANCE LEVEL)
	LOWER	460	(MG/L)	(1% SIGNIFICANCE LEVEL)
24H	GREATER	220	(MG/L)	(1% SIGNIFICANCE LEVEL)
--	LOWER	460	(MG/L)	(1% SIGNIFICANCE LEVEL)
48H	GREATER	220	(MG/L)	(1% SIGNIFICANCE LEVEL)
	LOWER	460	(MG/L)	(1% SIGNIFICANCE LEVEL)
72H	GREATER	220	(MG/L)	(1% SIGNIFICANCE LEVEL)
	LOWER	460	(MG/L)	(1% SIGNIFICANCE LEVEL)
96H	GREATER	220	(MG/L)	(1% SIGNIFICANCE LEVEL)
	LOWER	460	(MG/L)	(1% SIGNIFICANCE LEVEL)

SYMPTOMS :

NARCOTIC-LIKE STATE, TUMBLING

NO OBSERVED EFFECT CONCENTRATION: 100 MG/L

MAXIMUM CONCENTRATION CAUSING NO MORTALITY: 215 MG/L

MINIMUM CONCENTRATION CAUSING 100% MORTALITY: 464 MG/L

Kirsch Aug 19, 1988

DR.MED.VET. P.KIRSCH
HEAD OF SECTION

Munk, Aug. 17, 1988

DR.RER.NAT. R.MUNK
STUDY DIRECTOR

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TEST SUBSTANCE:

TEST SUBSTANCE NO.: 87/406

NAME OF TEST SUBSTANCE: SOLVENON PP

DEGREE OF PURITY: 100%

HOMOGENEITY: ENSURED SINCE THE TEST SUBSTANCE IS A GENUINE LIQUID

SOLUBILITY IN WATER: SLIGHTLY SOLUBLE ACCORDING TO SPONSOR
(CF. REMARKS P. 6)

CHARACTERIZATION: DETAILS ON THE CHARACTERIZATION ARE INCLUDED
IN THE RAW DATA AND MAY BE REQUESTED FROM THE
SPONSOR.

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METHOD:

THE METHOD USED CLOSELY FOLLOWED THE GUIDELINE OF DIN 38 412 "TESTVERFAHREN MIT WASSERORGANISMEN (GRUPPE L). ALLGEMEINE HINWEISE ZUR PLANUNG, DURCHFUEHRUNG UND AUSWERTUNG BIOLOGISCHER TEST-VERFAHREN (L1)" UND "BESTIMMUNG DER WIRKUNG VON WASSERINHALTSSTOFFEN AUF FISCHE - FISCHTEST (L15)", JUNE 1982, USING A STATIC PROCEDURE.

PHOTOPERIOD: 16 HOURS LIGHT AND 8 HOURS DARKNESS

REASONS FOR THE SELECTION OF THE CONCENTRATIONS:

BASED ON THE RESULTS OF A RANGE FINDING STUDY (LC 50 AFTER 96 H: BETWEEN 100 AND 1000 MG/L) THE CONCENTRATIONS, SPACED BY A FACTOR OF ABOUT 2.2, WERE FIXED AS FOLLOWS:
100, 215, 464 AND 1000 MG/L.

AERATION: SLIGHT

PREPARATION OF THE TEST SUBSTANCE: THE PRODUCT WAS ADDED TO THE TEST WATER WITHOUT ANY PRETREATMENT; SUBSEQUENTLY THE FISH WERE PLACED INTO THE AQUARIA.

RETENTION OF RECORDS:

THE RAW DATA AND THE ORIGINAL OF THE REPORT ARE STORED IN THE
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